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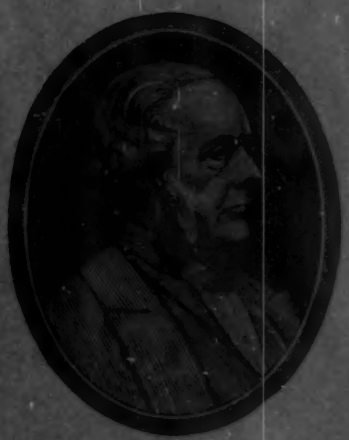

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THE
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THE SURGICAL TREATMENT OF CARCINOMA OF THE HYPOPHARYNX

BY RONALD W. RAVEN, O.B.E., LONDON

IN the treatment of carcinoma of the hypopharynx I believe that radical surgery has an important place. For some patients it is the only treatment which can be advised even though the disease has spread to the regional lymph-nodes, and others can be helped when radiotherapy has failed. This opinion is based on my experience derived from the surgical treatment of a series of 24 patients with proved squamous carcinoma, half of whom had metastases in the regional lymph-nodes, many were suffering from dyspnœa, stridor, or dysphagia, and 4 had received radiotherapy. In the management of these patients who are seriously ill there are a number of surgical problems to overcome, and in this paper the technical details of the operations which I have performed are described together with the methods whereby some of the difficulties can be overcome. In addition the end-results achieved in this series are presented. The term hypopharynx is used in its widest sense to include the region of the hypopharynx which extends from the glosso-epiglottic fold to the pharyngo-œsophageal junction. (*Fig.* 122.)

Table I.—AGE INCIDENCE

YEARS	37–39	40–45	46–50	51–55	56–60	61–65	66–70	71–75
No. of patients	2	0	2	1	6	7	5	1

Sex and Age Incidence.—There were 11 males and 13 females distributed in the age groups shown in *Table I*; the youngest patient was 37 and the oldest 75.

Assessment of Operability.—Before radical surgery is undertaken a full investigation of the general and local condition of the patient is made. The final decision not to operate is taken only after a careful assessment of the situation, knowing that it removes the patient's only hope. On the other hand, surgery must not be attempted if the patient is left worse off afterwards. An associated lesion such as myocardial degeneration may be present and consultation with a physician is necessary before the desirability or otherwise of an operation is determined. As much information is obtained as is possible to assess the extent of the disease in the pharynx. A long history usually means advanced disease; in these patients the hypopharynx may be fixed with lateral extensions into the neck, and immobile hard lymph-nodes are present which preclude a radical operation (*Fig.* 123). Even when the regional lymph-nodes contain metastases but are still mobile I have found that a satisfactory result can be achieved by surgery. Pharyngoscopy reveals the upper limit of the growth, and though it reaches the root of the tongue this, as a single factor, does not contra-indicate operation, but if it extends higher in the wall of the oro- or nasopharynx the disease is inoperable. Laryngoscopy shows any anterior extension into the larynx and this, or any tracheal extension, can be dealt with satisfactorily. Radiological examination of the neck with plain X rays, a barium swallow, and tomograms gives additional information regarding the extent of the disease (*Figs.* 124, 125). The barium picture may show some involvement of the cervical œsophagus, but this is accurately determined when the neck is explored, and at the same time any posterior extension into the prevertebral muscles is also found.

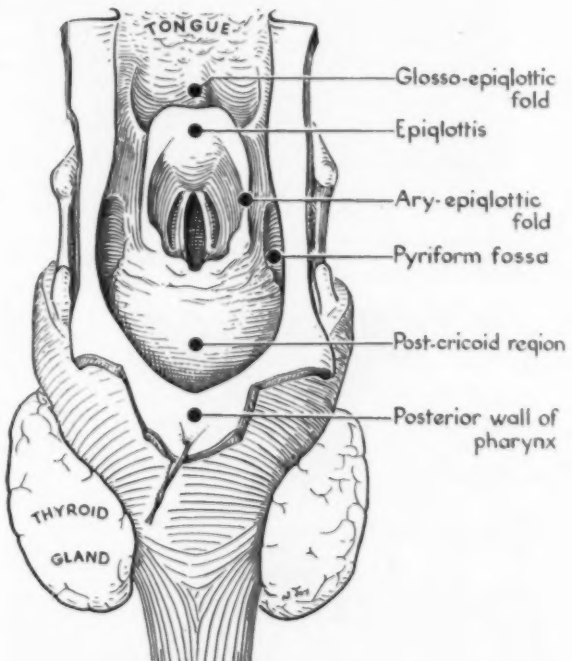

FIG. 122.—Drawing of the hypopharynx showing the sites in the mucous membrane where, according to Trotter, carcinoma commences.

The latter rendered the condition inoperable in 1 patient and a palliative tracheotomy and gastrostomy were therefore performed.

FIG. 123.—Clinical photograph of a patient with an inoperable carcinoma of the hypopharynx with enlarged fixed cervical lymph-nodes.

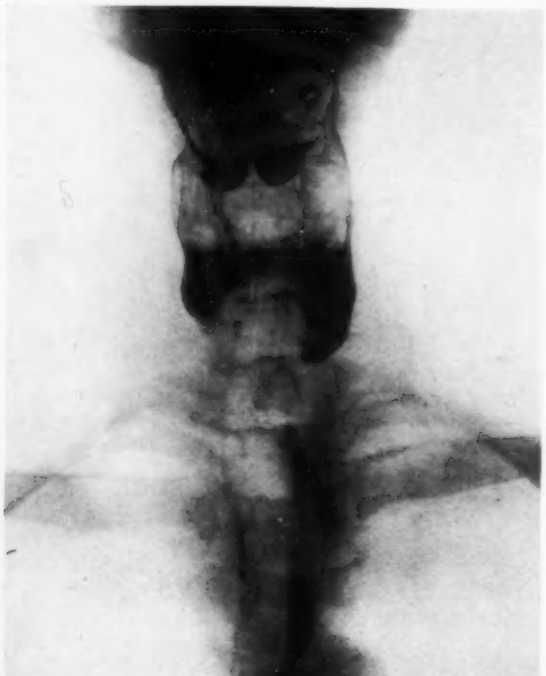

FIG. 125.—X-ray photograph of the hypopharynx and upper œsophagus after swallowing barium in a patient with a post-cricoid carcinoma causing a severe stricture.

Extent of the Radical Operation.—This is governed by the way the disease develops and spreads, and I studied autopsy material and specimens removed by operation to learn these facts so that it could be eradicated by the following procedure based on them.

The larynx and hypopharynx with the cervical œsophagus when necessary are removed with the regional lymph-nodes as a monoblock operation. For the higher growths the hyoid bone is removed and when the cervical œsophagus is affected it is divided at the thoracic inlet. If possible 2·5 cm.

FIG. 124.—X-ray photograph of the neck of a patient with an extensive carcinoma of the hypopharynx invading the trachea, showing a large soft-tissue shadow.

of healthy tissue should separate the line of section from the macroscopic edge of the growth; if there is any doubt regarding clearance immediate histological examination by the frozen-section technique is done. When the lateral lobes of the thyroid gland are invaded, total thyroidectomy is necessary. The trachea is divided between the second and third rings for the higher growths and between the third and fourth, or lower down, for the inferior lesions.

Careful attention is given to the regional lymph-nodes in every patient (*Fig.* 126). Most of the lymphatic vessels of the hypopharynx are included in the supraglottic pedicle and enter the deep cervical lymph-nodes around the internal jugular vein which extend from the level of the posterior belly of the digastric to the omohyoid muscles. Separate lymphatic vessels also pass from the posterior pharyngeal wall to the same lymph-nodes. If the larynx and trachea are invaded by the growth there may be additional metastases in the prelaryngeal and pretracheal lymph-nodes. When the cervical œsophagus is invaded, the lymph-nodes around the recurrent

laryngeal nerves may contain metastases (*Fig.* 127). Accordingly they are all examined at the operation, and I have found that they are usually larger on one side where I carry out a radical block dissection including the internal jugular vein, sternomastoid, and posterior belly of the digastric muscle. If they

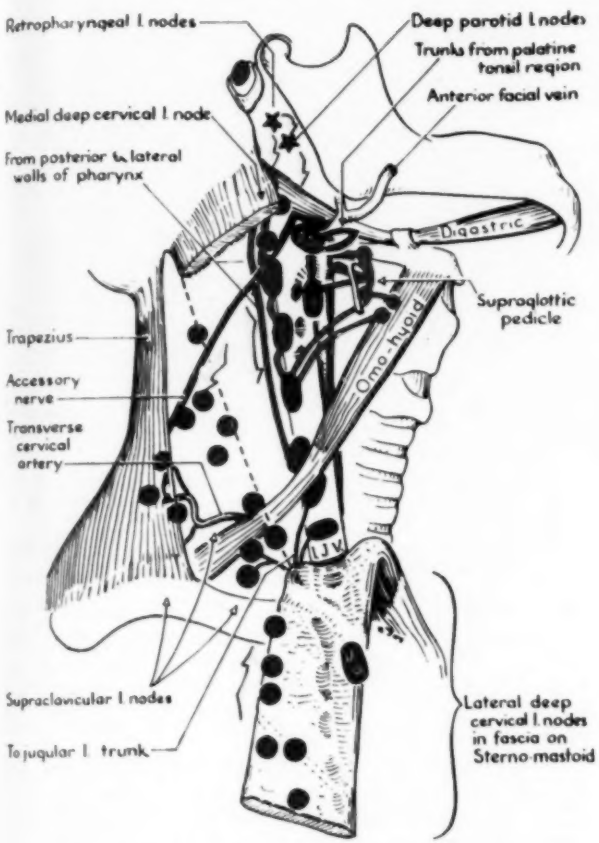

FIG. 126.—Scheme of the lymphatics of the mucous membrane of the pharynx.

Key to Diagram: *Yellow ochre*, Routes from one group of lymph-nodes to another. *Blue*, Routes from the palatine tonsil region. *Red*, Routes draining the hypopharynx through the supraglottic pedicle. *Green*, Routes from the posterior and lateral walls of the pharynx which pierce the posterior wall in the midline. J.D., Jugulo-digastric lymph-node. J.O., Jugulo-omohyoid lymph-node. I.J.V., Internal jugular vein.

are enlarged but smaller on the other side I remove them carefully, but leave this internal jugular vein and sternomastoid muscle whenever possible. Failure to remove any affected regional lymph-nodes in both sides of the neck may mean early recurrent disease.

Certain Pre-operative Considerations.—A preliminary tracheotomy should be avoided if possible because it will cause infection in the root of the neck, which makes the radical operation more difficult. When dyspnœa is present spraying the pharynx and larynx with cocaine solution often causes a severe exacerbation and this may require an immediate tracheotomy. For these patients I defer direct pharyngoscopy and laryngoscopy until the patient is in the operation theatre for the major procedure, when a biopsy and histological examination by the frozen-section technique is also done. For the same reason I have deferred the extraction of carious teeth until after the major operation has been performed. When respiratory distress is present I institute a tracheotomy under local anæsthesia as the first step in the radical operation, which is then continued under endotracheal anæsthesia. If severe dysphagia has caused marked dehydration and wasting a temporary gastrostomy is required to build up the patient's nutrition for three weeks before the

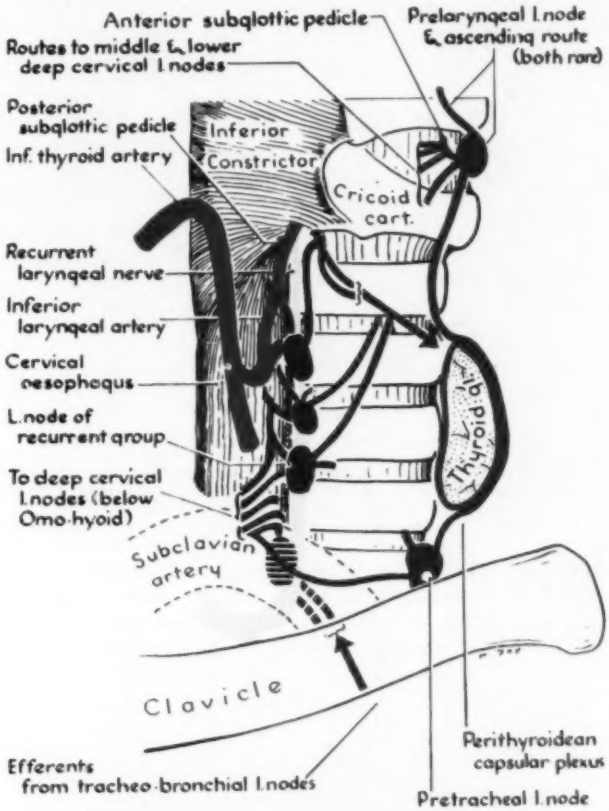

FIG. 127.—Scheme of the lymphatics of the cervical segment of the œsophagus, subglottic region, of the larynx and the upper end of the trachea.

Key to Diagram: *Yellow ochre*, Routes from one group of lymph-nodes to another. *Blue*, Perithyroid capsular lymph-plexus. *Green*, Routes draining cervical œsophagus, upper end of the trachea, and the region below the true vocal cords, to the lymph-nodes.

radical operation is done. Information is given to the patient regarding the permanent tracheostomy and the two stages of the operation which necessitates tube feeding for a time. If the patient can talk to another who has undergone this operation it is a great help and I try to arrange that this is done.

TECHNIQUE OF THE RADICAL TWO-STAGE OPERATION: LARYNGO-PHARYNGECTOMY AND LARYNGO-ŒSOPHAGO-PHARYNGECTOMY

I have carried out this procedure for the majority of the patients and found it very satisfactory.

1. Excisional Stage.—

Anæsthetic.—Induction is effected with intravenous pentothal sodium and an endotracheal tube with inflatable cuff is passed gently into the trachea so that the growth is not injured. The cuff of the

tube is inflated with air, and endotracheal nitrous-oxide gas and oxygen are then administered. Care is taken that the tube is not inserted so far as to

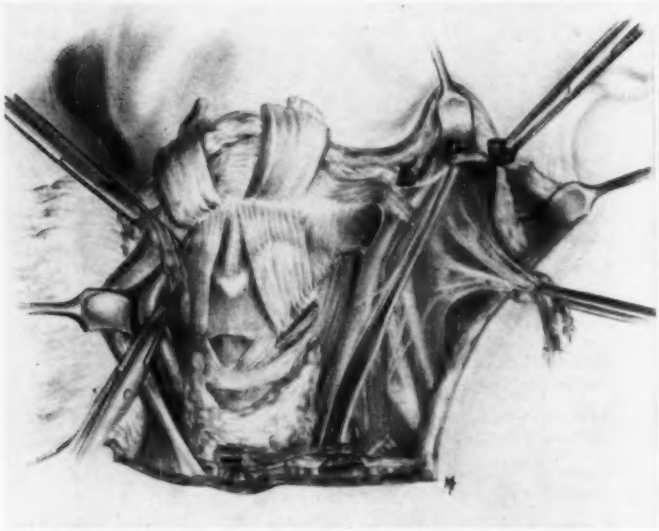

FIG. 128.—Laryngo-œsophago-pharyngectomy. Drawing of the early steps in the operation—block dissection of the lymph-nodes has been done on the left side (for clarity they are drawn away from the pharynx) and a limited dissection is being completed on the right side. The infrahyoid muscles are divided and the inferior and middle thyroid veins ligated.

occlude a bronchus. Sometimes intubation is not possible because of a large growth and extensive œdema, and it is then necessary to perform the first steps of the operation under local anæsthesia with

FIG. 130.—Laryngo-œsophago-pharyngectomy. Excision of the larynx, hypopharynx, and cervical œsophagus is complete; the epiglottis is being removed. The right sternomastoid is sutured to the prevertebral muscles.

the object of dividing the trachea as soon as possible to allow a general anæsthetic to be given.

Skin Incision.—A quadrilateral skin-flap based on the sternomastoid muscle not being removed is marked out on the neck. The upper horizontal incision crosses the neck from the anterior border of the sternomastoid to the posterior border of the opposite sternomastoid at the level of the hyoid bone; the lower horizontal incision crosses ½ in. above the

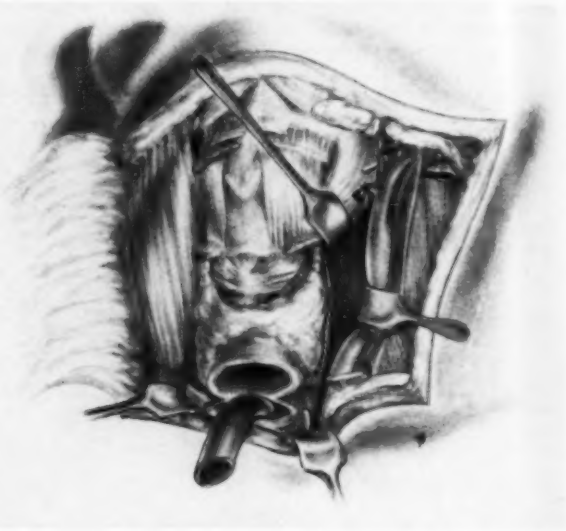

FIG. 129.—Laryngo-œsophago-pharyngectomy. Later steps in the operation showing mobilization of the hypopharynx after ligation of left superior and inferior thyroid arteries and division of left superior and recurrent laryngeal nerves. The same is done on the right side, the trachea is divided and the anæsthetic is continued through the tracheostomy.

suprasternal notch from the clavicular head of the sternomastoid to the level of the midpoint of the clavicle. A vertical incision connects them, and the flap is then reflected off the platysma to the anterior border of the sternomastoid and it is covered by hot packs throughout the operation.

Assessment of the Disease.—This involves an examination of the regional lymph-nodes in both sides, any involvement of the thyroid gland and cervical œsophagus is determined by palpation, and the degree of mobility of the hypopharynx is noted. Sometimes the lumen of one internal jugular vein is invaded by the growth and is pulled over to become closely attached to the pharynx.

Dissection of the Regional Lymph-nodes.—This step has been discussed already; the lymph-nodes and other tissues to be removed are dissected inwards and are left attached to the pharynx.

Mobilization of the Hypopharynx (*Fig.* 128).—The origins of the sternothyroid and sternohyoid muscles and the posterior belly of the omohyoid are divided, and the following blood-vessels are ligated and divided: the middle and inferior thyroid veins, and the superior and inferior thyroid arteries. The superior and recurrent laryngeal nerves are then divided and by blunt dissection the posterior wall of the hypopharynx is freed from the prevertebral fascia to a level of just below or above the hyoid bone, depending on the extent of the growth (*Fig.* 129). When the cervical œsophagus requires removal it is mobilized to the thoracic inlet. The vessels and nerves on the opposite side are dealt with in the same way, the lateral compartments of the neck are protected by hot swabs, and all is ready for the resection.

Division of the Trachea.—When a high growth is present, I divide the trachea between the second and

third rings; in low growths, between the third and fourth rings, or lower if necessary. The endotracheal tube with inflatable cuff is then introduced through the tracheostomy for the anæsthetic to continue. The anterior rim of the tracheostomy is fixed to the skin by interrupted sutures of nylon.

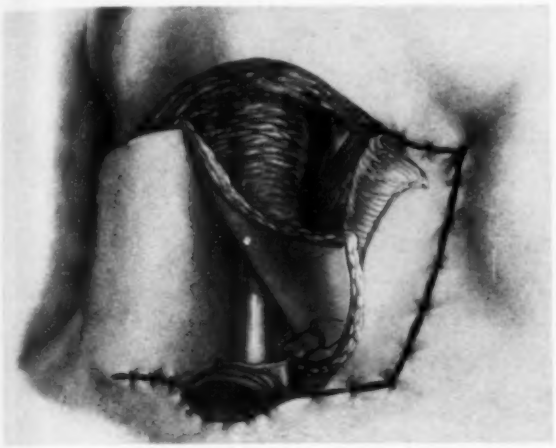

FIG. 131.—Laryngo-œsophago-pharyngectomy. Reconstructional stage—first phase. The anastomosis between the mucous membrane of the upper divided hypopharynx and the quadrilateral skin-flap is complete; the anastomosis between the skin-flap and cervical œsophagus is being done. A polythene tube has been passed into the stomach for feeding purposes.

Division of the Cervical Œsophagus (*Fig.* 130).—When there is doubt regarding the exact upper limit of the carcinoma, the pharynx is opened through a normal part of its wall and the interior is inspected so that it can be divided at a satisfactory level away from the growth. In high growths a suprahyoid division is necessary, but in lower ones it is resected at the level of the thyrohyoid membrane. The mucous membrane covering the upper border of the epiglottis is conserved for the reconstruction, but the rest of this structure is removed.

2. Reconstructional Stage.—

First Phase (*Fig.* 131).—This is completed at the same operation. If one sternomastoid muscle remains its anterior border is sutured to the prevertebral fascia to shut off the lateral compartment on that side of the neck.

Formation of the skin hypopharynx: The quadrilateral skin flap is laid over the prevertebral tissues and the posterior wall of the œsophagus is sutured to its lower border with interrupted sutures of alternate fine nylon and catgut placed ½ in. apart. In a similar way the posterior wall of the divided hypopharynx is sutured to the upper border of the skin-flap. The skin-flap is then turned on itself to make a tube, the anterior wall of the œsophagus is sutured similarly to its lower border, and the anterior wall of the hypopharynx to its upper border. The longitudinal lateral opening is left temporarily and the other skin edges are approximated, the raw area in the lateral aspect of the neck and over the skin tube is covered with a split-thickness skin-graft taken from the inner side of the thigh.

Insertion of tubes: A polythene tube is passed through the œsophagostomy into the stomach for feeding purposes. A tube is inserted in the tracheostomy, a small roll of gauze is placed in the new skin tube, and dressings are applied for healing to occur, and during this time the new skin hypopharynx will develop an additional blood-supply from the prevertebral region.

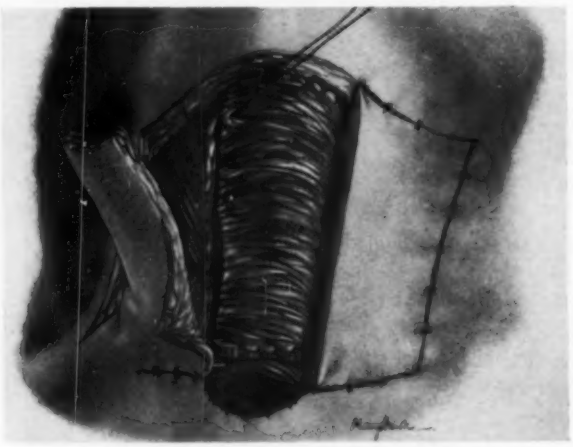

FIG. 132.—Laryngo-œsophago-pharyngectomy. Reconstructional stage—second phase. The lateral cervical fistula is being closed to form a new skin hypopharynx. This is covered by a rotation skin-flap from the lateral aspect of the neck.

Second Phase.—

Closure of the lateral cervical fistula (*Fig.* 132): A longitudinal incision is made through the skin on the posterior aspect of the fistula and the medial part of it is mobilized so that it will lie in easy apposition with the anterior wall. The skin edge of the latter is freshened and the opening is closed with interrupted alternate sutures of nylon and catgut placed ½ in. apart. This completes the formation of the skin hypopharynx.

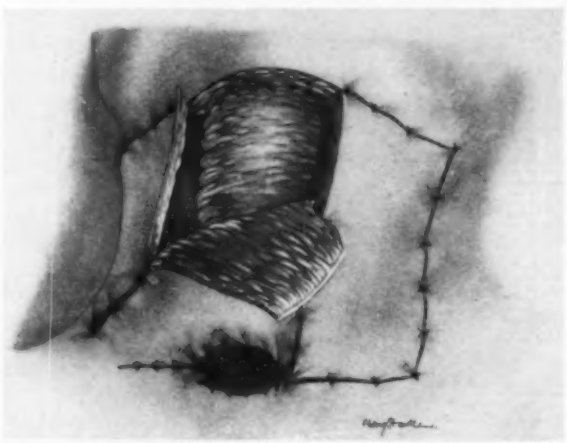

FIG. 133.—Laryngo-œsophago-pharyngectomy. Reconstructional stage—second phase. The rotation skin-flap is being sutured to provide whole-thickness skin cover for the new skin hypopharynx. The raw areas in the neck are covered with split-thickness skin from the thigh.

Skin cover for the new hypopharynx (*Fig.* 133): The skin tube is covered by full-thickness skin obtained by a rotation skin-flap from the lateral aspect of the neck; the resulting raw area is covered by a split-thickness skin-graft taken from the thigh.

FIG. 134.—Clinical photograph of a patient after laryngo-œsophago-pharyngectomy who is well 51 months later.

FIG. 135.—X-ray photograph after swallowing barium (patient in *Fig.* 134).

FIG. 136.—Photograph of the specimen removed in the case of patient shown in *Fig.* 134. The carcinoma extends from the arytenoid region to the cervical œsophagus.

Sometimes the skin on the side of the neck can be undermined sufficiently so that it can be pulled over and sutured to the opposite side.

Insertion of a Ryle's tube : A Ryle's tube is passed through the nose into the stomach for feeding purposes until the wounds have healed. A tube is inserted in the tracheostomy and dressings are applied to the wounds.

Post-operative Treatment.—

After the First Stage.—During the initial 48 hours the patient has special day and night nurses. Blood transfusion, commenced during the operation, is continued afterwards, and usually 1 pint is sufficient, but this depends upon the patient's general condition. A suction pump is placed at the bedside to aspirate tracheal secretions at intervals. Severe dyspnœa and tachycardia usually mean tracheal or bronchial obstruction by secretions, which is relieved by suction from a strong pump. Nutrition is maintained by intravenous infusions for the initial 24 hours until the possibility of anæsthetic vomiting has gone, when tube-feeding is commenced, the daily caloric intake being 3000, with additional vitamins and iron. Penicillin is given systemically until the temperature settles after a few days. At the end of 48 hours the neck is dressed without disturbing the skin graft, which is left for five days. The usual wound toilet is carried out and pledgets of cotton-wool soaked in a mixture of equal parts of icthyol and zinc cream are placed in the skin tube and gauze soaked with this solution is laid around the tracheostomy to protect the skin from secretions. Gauze is placed behind the tracheostomy tube to prevent saliva entering the trachea. During the

interval before the second stage is done the patient is built up, graded exercises are taken, occupational therapy is given, a writing pad is provided as the patient cannot speak, and everything is done to maintain the morale.

FIG. 137.—Clinical photograph of a patient after laryngo-œsophago-pharyngectomy who is well 29 months later.

FIG. 139.—Photograph of the specimen removed in the case of the patient shown in *Fig.* 137. The carcinoma extends from a point inferior to the arytenoids to the cervical œsophagus. The œdema of the arytenoid region is shown.

After the Second Stage.—During the initial 24 hours, nutrition is maintained by intravenous infusion and afterwards routine tube-feeding is carried out. The usual treatment is given to the wounds, which should heal in two or three weeks, when normal swallowing is resumed. A metal shield is provided to cover the tracheostomy by day, and the patient usually prefers to wear a tube by night. Speech therapy is also given, but talking is not so good as after laryngectomy. Normal dress for the neck should be worn. (*Figs.* 134–139.)

Post-operative fistula: This troublesome complication sometimes occurs as a result of local skin

FIG. 138.—X-ray photograph after swallowing barium (patient in *Fig.* 137).

necrosis and there are two varieties—namely, high and low. The former occurs in the hyoid region and the latter between the hypopharynx and trachea. A high fistula developed in a patient aged 75, which I closed by the following technique (*Figs.* 140—142): A quadrilateral flap of mucous membrane was reflected downwards from the root of the tongue and joined with interrupted catgut sutures to the freshened edge of the inner skin lining of the new hypopharynx. This was then covered by the full-thickness skin of an acromiopectoral tubed pedicle graft which had been prepared previously. Primary healing occurred and the patient swallowed normally afterwards. A low fistula may be caused sometimes by a rigid tracheotomy tube pressing against the posterior tracheal wall, and is prevented by placing a gauze dressing behind the tube until healing is sound. When it is small, gradual contraction with spontaneous closure usually occurs; while this is taking place a strip of gauze is placed over it and is held in position by the tracheotomy tube, thereby closing the opening, and permits the patient to swallow. If the fistula is large a plastic operation to close it may be required or alternatively a portex tube is inserted in the hypopharynx and into the upper œsophagus beyond the opening, thus giving time to see if it will heal; in the meantime the patient is allowed to swallow.

RADICAL OPERATION AFTER UNSUCCESSFUL RADIOTHERAPY

After treatment with irradiation a number of technical difficulties are created, especially in the reconstruction operation, because of the severe impairment in the vitality of the skin of the neck. I have found two techniques of value in dealing with them, but the same principles of the radical operation must always be observed.

FIG. 140.—Clinical photograph of a patient, aged 75, after laryngo-œsophago-pharyngectomy to show a high fistula.

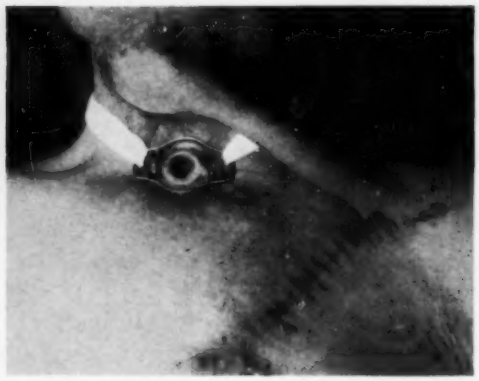

FIG. 141.—Clinical photograph of the same patient (*Fig.* 140) showing the acromiopectoral tubed pedicle skin-graft in position.

FIG. 142.—Clinical photograph of the same patient (*Figs.* 140, 141) after successful closure of the fistula. He died, after 30 months, of other cause.

for the skin of the neck to improve before it is closed, and a portex tube is inserted in the hypopharynx and beyond the fistula into the œsophagus, so that the patient can swallow in the meantime (*Fig.* 143). Several months may be required before the tissues have recovered sufficiently for the final plastic operation for closure to be done, and during this time bilateral acromiopectoral tubed pedicle grafts are prepared. To close the fistula it may be possible

FIG. 143.—Clinical photograph of a patient who has undergone operation after unsuccessful radiotherapy, showing the median pharyngeal stoma with the portex tube in position. Note the extensive irradiation changes in the skin of the neck.

FIG. 144.—Clinical photograph of the same patient (*Fig.* 143), showing the right acromio-pectoral tubed pedicle skin-graft in position; the left one is in reserve.

FIG. 145.—Clinical photograph of the same patient (*Figs.* 143, 144) after successful closure of the fistula. The patient is well after 30 months.

1. Conservation of a Strip of the Posterior Pharyngeal Wall.—When the carcinoma is situated away from the posterior wall of the hypopharynx it is possible to leave a strip of this wall and suture its edges to the skin of the neck to form a median pharyngeal fistula. A suitable interval is allowed to use a quadrilateral full-thickness flap turned over, hinged on one edge of the fistula, and sutured to the opposite edge to provide the inner skin lining. This is then covered by full-thickness skin from an acromiopectoral tubed pedicle graft (*Figs.* 144, 145). Alternatively, both acromiopectoral grafts may be required for the inner skin lining and outer skin cover.

2. Use of a Narrow Quadrilateral Skin-flap.—When the whole of the hypopharynx must be removed, the quadrilateral skin-flap should be made sufficiently narrow to cover the prevertebral tissues and form a posterior wall for the skin pharynx. It will probably retain a sufficient blood-supply to survive in these circumstances. Its upper border is sutured to the posterior wall of the divided hypopharynx, the lower border to the posterior wall of the divided œsophagus, and the free edge to the skin of the opposite side of the neck. The mucous membrane of the anterior wall of the cut pharynx is sutured to the skin of the submaxillary region and the patient is left temporarily with a posterior skin gutter. Acromiopectoral tubed pedicle grafts are then prepared from which the anterior wall of the skin pharynx is reconstructed in stages, and full-thickness skin cover is provided for it (*Figs.* 146–148).

FIG. 146.—Clinical photograph of a patient with a carcinoma of the hypopharynx after unsuccessful radiotherapy. He has a palliative tracheotomy and severe dermatitis of an extensive area of skin.

FIG. 147.—Clinical photograph of the same patient (*Fig.* 146) during the reconstruction of the new skin hypopharynx, using acromiopectoral tubed pedicle skin-grafts.

FIG. 148.—Clinical photograph of the same patient (*Figs.* 146, 147) showing the end-result. He is well 29 months later.

FIG. 149.—Clinical photograph of a patient after laryngo-pharyngectomy with end-to-end anastomosis; the patient had a fixed cervical kyphosis which made this possible. He died of cancer after 20 months.

FIG. 150.—Clinical photograph of a patient after partial pharyngectomy with conservation of the larynx. She died of cancer after 23 months.

ONE-STAGE OPERATIONS WITH PRIMARY CLOSURE OF THE PHARYNX

I have performed several procedures for patients when the extent of the disease was limited. The same rules apply to the treatment of the regional

lymph-nodes as stated for the radical two-stage operation. These one-stage operations are not so radical and recurrence is therefore more likely even though the patients are carefully selected, so I prefer the more radical two-stage operation.

1. Laryngo-partial Pharyngectomy.—A sufficient width of the posterior pharyngeal wall is left after the parts are excised to reconstruct a tube of mucous membrane and reinforce it with fibromuscular tissue. The skin of the neck is then closed over it.

2. Laryngo-pharyngectomy with End-to-end Anastomosis.—I was able to perform this operation in one patient with a severe fixed cervical kyphosis, which made it possible to anastomose the upper divided hypopharynx with the pharyngo-œsophageal junction by an end-to-end procedure. The skin of the neck was closed, the wounds healed well, and the patient swallowed perfectly after five weeks (*Fig.* 149).

3. Partial Pharyngectomy with Conservation of the Larynx.—When a small carcinoma is localized in the lateral wall of the hypopharynx, wide local resection can be done with reconstruction of the pharynx and the patient is left with a normal larynx (*Fig.* 150).

4. Resection of the Hypopharynx with Conservation of the Larynx.—One patient with a post-cricoid carcinoma was averse to losing her larynx, and I therefore removed the hypopharynx only and constructed a new one of skin, anastomosing it to the oropharynx above and the œsophagus below. The functional result was bad, as fluid also passed into the larynx on swallowing, and I had to perform a gastrostomy. She died one year later from recurrence. I believe that the larynx must be removed with the hypopharynx on account of the risk of recurrent disease.

END-RESULTS WITH SURGICAL TREATMENT

The survival periods for 23 patients following all types of excisional surgery described in this paper are set out in *Table II*. There was no operative mortality in the series. An additional patient proved to have inoperable disease on exploration of the neck, and a palliative tracheotomy and gastrostomy were instituted.

When the results of surgical treatment are considered, a number of facts must be taken into account in addition to survival periods. Each patient has serious symptoms which require immediate relief, and this presents a specific problem. In many patients with dyspnœa or stridor I have found the disease in the hypopharynx so extensive with infiltration of the larynx and thyroid, and regional lymph-node metastases, as to render it unsuitable for irradiation treatment. No treatment other than surgery was therefore possible for the majority of my patients, who were thereby relieved of distressing symptoms and given the possibility of more permanent benefit. After operation they are happy, grateful, dress normally, and are able to live useful lives. Some of them have returned to work. They swallow everything easily and no one has developed a fibrous stricture at the junction of the skin pharynx with the œsophagus or elsewhere. They are not able to speak so well as after laryngectomy, but a number are able to be understood.

Table II.—END-RESULTS OF ALL TYPES OF OPERATION (FOLLOW-UP JUNE 30, 1953)

	PERIOD IN MONTHS AFTER OPERATION											
8 patients alive	9	12	14	29	29	30	32	51	—	—	—	—
12 patients died of cancer	4	4	6	8	8	12	12	12	20	23	23	33
3 patients died of other cause	2	10	30	—	—	—	—	—	—	—	—	—

The longest survival period at present is 51 months. This patient, aged 67, had an extensive carcinoma causing severe dysphagia, for which a gastrostomy was performed elsewhere, and she remains well and swallows perfectly—the gastrostomy was allowed to close.

I wish to thank all who have helped me in this work: my anæsthetists, Dr. L. H. Morris and Dr. A. M. Chester; my surgical registrars and house surgeons; and the nursing staffs, for their skilful work. Dr. J. W. Whittick and Dr. J. H. O. Earle assisted me with the pathological aspects. I am grateful to Miss J. Hunt and Dr. P. Hansell, of the photographic departments of the Royal Cancer Hospital and Westminster Hospital respectively, for the clinical photographs and Miss M. Hawker and Miss N. Joy for the drawings. Portland Plastics Ltd. kindly supplied me with portex tubes.

REFERENCES

CUNNINGHAM, D. J. (1951), *Textbook of Anatomy* (ed. J. C. Brash), 9th ed. London: Oxford Medical Publications.

DELAMERE, G., POIRIER, P., and CUNÉO, B. (1903), *The Lymphatics* (trans. C. H. Leaf). Westminster: Archibald Constable & Co., Ltd.

RAVEN, R. W. (1952), *Brit. med. J.*, **1**, 951.

ROUVIÈRE, H. (1932), *Anatomie des Lymphatiques de L'homme*. Paris.

TROTTER, W. (1929), *Brit. J. Surg.*, **16**, 485.

— — (1932), *Brit. med. J.*, **1**, 510.

SOME OBSERVATIONS ON FRACTURES OF THE HEAD OF THE RADIUS WITH A REVIEW OF ONE HUNDRED CASES

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EXPERIENCE has taught the surgeon in his approach to the injured elbow to regard this complicated hinge joint with trepidation and with great respect.

The elbow-joint tolerates trauma very badly. Even a minor injury can be responsible for some residual loss of range of movement of the joint.

Fractures of the head of the radius have been variously estimated as forming 17 per cent (Jones, 1935) and 44 per cent (Murray, 1940) of all elbow injuries.

A survey in this area of all elbow fractures and dislocations, including the supracondylar fracture of the humerus of children, reveals some 30 per cent of fractures of the head of the radius.

ANATOMICAL CONSIDERATIONS

The head of the radius very grossly resembles the structure of the patella, consisting of the columnar type of dense cancellous bone running in a more or less longitudinal pattern. In consequence, fractures of the radial head tend to be oblique or longitudinal in direction. The head and its articular circumference are intra-articular, the articular circumference being deepest on the medial side where it articulates with the radial notch of the ulna.

During the flexion and extension movements of the elbow, the radial head glides to and fro over the capitellum of the humerus. The capitellum and the radial head are reciprocally curved; but actual contact between the surfaces is only present when the elbow is flexed to 130°, and the radius is in the mid-prone position. This can be demonstrated at operation and by dissection of the cadaver when the separation between the articular surfaces may be as much as ¼ in.

This consideration is of great importance. It means that in order for the flexion or extension range of movement of the joint to be limited, a moderately severe mechanical interference with this gliding motion must be present.

Cadaveral dissection and operation on the elbow-joint also reveal that full rotation at the proximal radio-ulnar joint requires accurate anatomical position of the head of the radius in the radial notch of the ulna. This is a tightly-fitting pivot joint held in position by the annular ligament.

Although during the backward and forward movement of the radial head on the capitellum, the head of the radius is moved on the radial notch of the ulna, and the annular ligament is slewed backwards and forwards at the same time, complete contact between the articular circumference of the radial head and the radial notch is always maintained. The supination and pronation movements at the proximal radio-ulnar joint, as judged by rotation of the elbow, are each in the nature of an arc of 160°. This corresponds with 320° of the articular circumference of the radial head. That portion of the head of the radius which forms the last 40° (one-ninth) of the articular circumference on its lateral border does not articulate with the radial notch of the ulna. Theoretically, this would mean that if more than one-ninth of the lateral segment of the radial head is involved in the fracture, the range of rotation movement at the elbow-joint will be limited. This limitation will be further increased should the injury, by tilting the fractured sector, put out of line the tightly-fitting pivot radio-ulnar joint. This is only a theoretical consideration and its practical application will be discussed later.

MECHANISM OF THE INJURY

In what is probably one of the earliest detailed descriptions of this injury, Cutler (1926) states that direct trauma was responsible for the fracture of the radial head, and Flemming (1932) found that 75 per cent of his cases were caused by direct injury.

It is now generally agreed that indirect trauma through the long axis of the radius is the usual cause.

It is with great difficulty that the patients can recall the exact mode of falling other than that they may attempt to break fall with the hand.

Experimentally, if the ball of the hand of the cadaver is heavily struck, the wrist being pronated, fully dorsiflexed, and radially deviated with the elbow flexed to 130°, and held firmly in a vice, dislocations of the elbow-joint and Monteggia type of fractures can relatively easily be produced (Mason, 1953).

Dislocations of the elbow-joint associated with fractures of the head of the radius are of sufficient frequency that they may be considered as part of the same traumatic process.

These observations agree with those of Hein, who, in a discussion of Key's Report (1931), considered that dislocations of the elbow-joint and fractures of the head of the radius had a common origin. This important factor, I believe, has a bearing on the subsequent disability of the joint, and will be discussed later.

CLINICAL REVIEW

The purpose of this investigation is to follow up the end-results in 100 cases of fracture of the head of the radius treated by conservative and operative measures; to attempt to assess the loss of range of movement of the elbow-joint if present, in relation to the bony and soft-tissue injury suffered by it, and to discuss its significance. It is also intended to discuss the method of treatment adopted in relation to the final functional results.

Selection of Cases.—The 100 cases were selected at random. Only those patients were included in which the interval between the injury and the follow-up was twelve months or more. The epiphysial displacement and neck fractures of children and young adults were excluded. No patient was included who had also sustained dislocation of the elbow, or fracture of the other components of the joint, apart from minor chip fractures.

Each of the 100 cases was examined at a follow-up clinic. The function of the elbow was estimated, the actual range of movement of the joint measured in degrees, the presence of pain noted, and the interval between the injury and return to work recorded.

Sex Incidence.—There were 48 female patients and 52 male patients. Almost all the female patients were housewives and most of the males were engaged in work of a heavy nature.

FIG. 151.—*Case* M. E. Anteroposterior radiograph taken 19 months after the original 'subchondral' fissure fracture of the radial head. The elbow-joint is normal. The fissure fracture is still visible. This is the usual phenomenon in any intra-articular fracture where callus formation might interfere with joint function. Function of the joint was full.

Age Group.—The average age of the 100 patients was 31 years. Most were between the ages of 20 to 40 years, probably the period of greatest muscular activity.

The average interval between the follow-up and the injury was 26 months, the longest being 60 months and the shortest 12 months.

Classification of the Fractures of the Head of the Radius.—The fractures were classified into three clinical types corresponding with a description of the radiological findings. No compound fracture was included. No 'flake' fractures of the head were encountered.

Type 1.—*Fissure fractures or marginal sector fractures without displacement.*

This type consists of the 'subchondral' crack fracture, and of fractures involving a sector of the lateral quadrant of the head of the radius without displacement.

Type 2.—*Marginal sector fractures with displacement.*

This is the type in which a segment of the lateral border of the radial head is separated from the other quadrants, is impacted and depressed, or is tilted out of line.

Type 3.—*Comminuted fractures involving the whole head of the radius.*

The actual classification of the 100 cases is shown in *Table I.*

Table I.—CLASSIFICATION OF FRACTURES OF THE RADIAL HEAD IN 100 CASES

	NUMBER OF CASES	PERCENTAGE
Type 1: Fissure or marginal fractures without displacement	62	62
Type 2: Marginal sector fractures with displacement	20	20
Type 3: Comminuted fractures involving the whole head of the radius	18	18
TOTAL	100	

Most of the radiographs and all the clinical notes taken at the time of injury were available for inspection.

It will be seen from *Table I* that 62 cases (62 per cent) of fracture of the head of the radius were uncomplicated by displacement, whilst 38 cases (38 per cent) were associated with displacement of the fragments.

CLINICAL ANALYSIS OF CASE GROUPS

It was decided to analyse in detail the series of cases of each type of fracture and to correlate the treatments of these patients with the findings on clinical and radiological examination.

ANALYSIS OF THE 62 CASES OF TYPE 1 FRACTURE (*Fissure or Marginal Fractures without Displacement*)

ORIGINAL TREATMENT.—Each of these 62 patients had been treated conservatively.

The limb had been immobilized in a sling, or in a plaster-of-Paris cylinder with the elbow at 90° of flexion for an average of 16 days.

If by then the traumatic hæmarthrosis had been absorbed, active elbow exercises were commenced.

FINDINGS ON CLINICAL EXAMINATION.—

Pain in the Elbow-joint.—Fifty-six cases made no complaint of pain. Six cases complained of an occasional ache on the medial side of the joint.

There was no joint laxity, no tenderness over the medial ligament, and no abnormality of the distal radio-ulnar joint in any of the 62 cases. The 'carrying-angle' was normal in all cases.

Range of Movement of the Elbow-joint.—Forty-two cases had a full range of movement of the elbow-joint. Twenty cases showed an average of 8° loss of extension movement of the elbow-joint, but supination and pronation movements were full. The loss of extension range of movement was no disability.

Function of the Elbow-joint.—Each of the 62 patients had full function of the elbow-joint and was doing his normal work without disability.

RADIOGRAPHIC EXAMINATION OF THE ELBOW-JOINT.—Ten cases were subjected to X-ray examination. They were selected at random.

Typically the elbow-joint was normal. The articular plateau of the radius was not distorted and the lateral and medial joint surfaces were regular in outline. There was no evidence of osteo-arthritic change.

The fissure fracture of the plateau of the radial head was often still visible. This is the usual phenomenon in intra-articular fractures where callus and new bone formation might interfere with joint function.

Fig. 151 shows the radiograph of a normal elbow-joint with a 'subchondral' fissure fracture. The original injury had been sustained nineteen months previously. The fissure fracture is still visible.

Fig. 152 shows the original and subsequent (thirty months later) radiographs of a typical marginal sector fracture without displacement. The fracture has united and the elbow-joint appears normal.

TIME OFF WORK.—The average duration of time between the injury and resumption of normal work was 4·8 weeks. The housewife usually recommenced her duties at 3–4 weeks, whilst the heavy worker recommenced his at 5–6 weeks.

This analysis demonstrates that each of the 62 patients with a Type 1 fracture of the radial head treated on conservative lines had regained full function of the elbow-joint and returned to normal work in an average of 4·8 weeks.

Six patients complained of minimal discomfort on the medial joint aspect.

Forty-two patients showed a full range of movement of the joint.

Twenty patients showed an average loss of 8° of extension movement of the elbow-joint.

ANALYSIS OF THE 20 CASES OF TYPE 2 FRACTURE (*Marginal Sector Fractures with Displacement*)

ORIGINAL TREATMENT.—

1. *Cases treated Conservatively.*—Fifteen of these 20 cases had been treated on conservative lines as for Type I fracture :—

Seven of these 15 patients had a segmental fracture less than one-quarter of the articular circumference of the radial head with depression of the fractured portion below the joint line without tilting.

The remaining 8 patients had been judged 'borderline' cases.

These patients had sustained sector fractures of the radial head in which the lateral segment was comminuted, or tilted, and displaced below the joint surface.

The fracture involved one-quarter or more of the articular circumference of the head, but the distortion of the articular plateau was not considered of a degree which would interfere with joint movement.

These cases were thought to be on the borderline between conservative and operative treatment, and excision of the head of the radius was not undertaken.

2. *Cases treated by Operation.*—Five patients had been treated by early total excision of the radial head. In these cases the segmental fracture was greater than one-quarter of the circumference of the head of the radius. The fracture was depressed and tilted so as to distort the articular plateau of the radial head.

FINDINGS ON CLINICAL EXAMINATION.—

Pain in the Elbow-joint.—

1. *Cases treated conservatively* : Six of the 15 patients treated conservatively were pain-free. Nine of them complained of some pain in the region of the radial head and there was crepitus in this region on rotation of the joint. Eight of these 9 patients were the originally considered 'borderline' cases.

There was no pain over the medial joint ligament, no joint laxity, and no loss of 'carrying-angle' in any of these 15 cases. In all 15 cases the distal radio-ulnar joint was normal.

2. *Cases treated by operation* : The 5 patients treated by excision of the head of the radius made no complaint of pain in the joint. No undue laxity of the joint was demonstrable in any of them, and in each case the 'carrying-angle' and the distal radio-ulnar joint were normal.

Range of Movement of the Elbow-joint.—

1. *Cases treated conservatively* : Seven of the 15 patients treated by conservative measures had a full flexion movement, but extension range of the elbow-joint was limited by an average of 10° of movement, and supination and pronation range of the joint was limited by an average of 15° of each movement.

The 8 'borderline' cases had a full flexion range, but extension range was limited by an average of 15° of movement.

Supination and pronation range of the joint was limited by an average of 30° of each movement.

2. *Cases treated by operation* : The 5 patients treated by operative removal of the whole head showed an average loss of extension motion of 20°, but a full rotation range of movement of the elbow-joint.

Function of the Elbow-joint.—

1. *Cases treated conservatively* : Seven of the 15 conservatively treated cases had full function, and 3 labourers amongst them were back doing their normal heavy work. The 8 'borderline' cases had good function, but 4 of them were now doing work of a lighter nature.

The extension loss of 15° was no disability to them, but the lack of rotation by a total of 60° was a severe handicap, especially for heavy shovelling work, or work involving the use of a screwdriver.

2. *Cases treated by operation* : The 5 patients treated by total excision of the radial head all had returned to their normal work.

They were housewives, and the loss of the last 20° of extension of the elbow-joint was no handicap to them.

RADIOGRAPHIC EXAMINATION OF THE ELBOW-JOINT.—

1. *Cases treated Conservatively.*—Ten of the 15 cases were selected at random and subjected to X-ray examination. Five of these patients originally had sustained a sector fracture of the radial head consisting of less than one-quarter of the articular circumference with depression of the fragment and no tilting. Typically the elbow-joint was normal with no osteo-arthritic changes. *Fig.* 153 shows one of these cases. The original radiograph is that of a typical Type 2 fracture, whilst the subsequent radiograph taken 15 months later shows a healed fracture with a normal elbow-joint.

The other 5 patients were 'borderline' cases. In these cases the lateral joint compartment was distorted. The articular plateau of the radial head was irregular and osteo-arthritic changes were evident. The medial joint compartment appeared normal.

Fig. 154 shows the original and subsequent (27 months later) radiographs of a case considered initially as 'borderline'. The original fracture is well defined, and involves more than one-quarter of the radial plateau. It is comminuted and tilted out of line. The fracture has healed with gross distortion of the articular circumference and the plateau of the radial head.

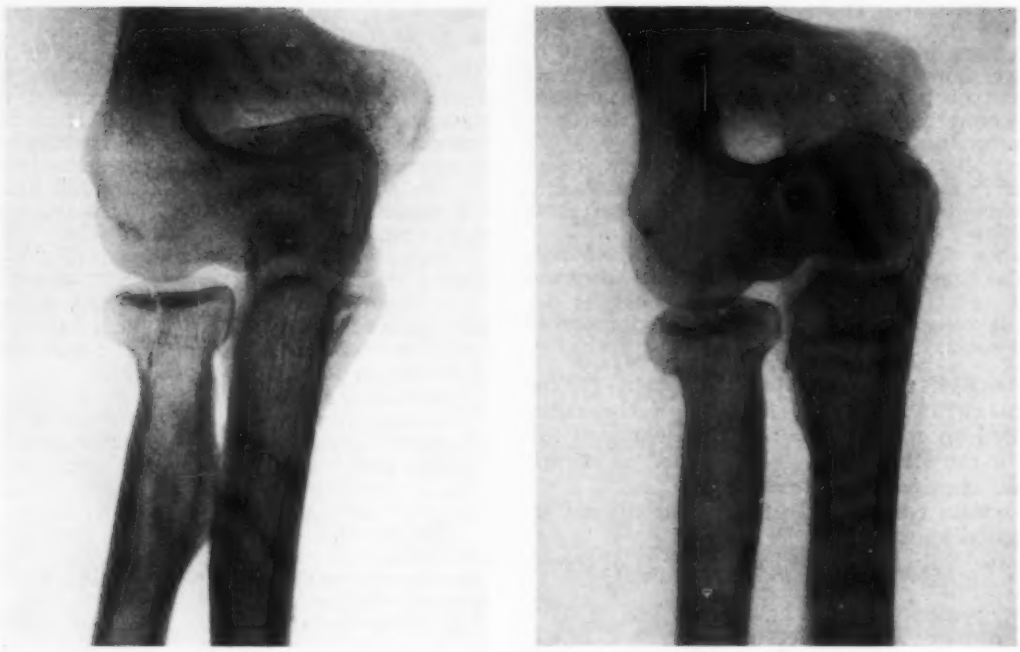
Fig. 155 shows the original and subsequent (42 months later) radiographs of another case of this group.

The fracture consists of one-quarter of the circumference of the head, but is tilted out of line. The subsequent radiograph shows a healed fracture with gross distortion of the radial head and early degenerative changes.

2. *Cases treated by Operation.*—Three of the 5 cases were subjected to X-ray examination. The radial head had been completely excised. The contour of the capitellum was normal and there was no osteo-arthritic change. Some new bone had formed around the neck of the radius.

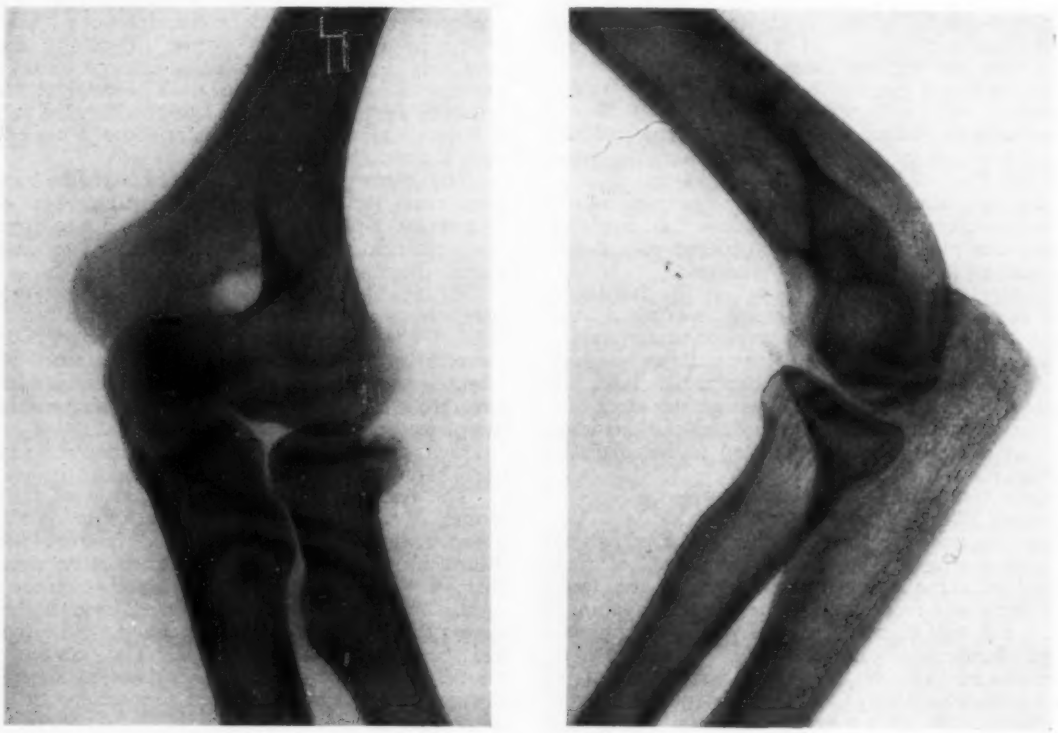
TIME OFF WORK.—

1. *Cases treated Conservatively.*—Seven of the 15 patients treated by conservative methods were back at their normal work in an average of 5 weeks from the time of the original injury.



A B

FIG. 152.—*Case* N. P. Anteroposterior radiographs showing a typical Type 1 fracture of the radial head. A, The original radiograph; B, The subsequent X-ray photograph taken 30 months later. The fracture has united and the elbow-joint appears normal. The function of the joint was full.



A. B

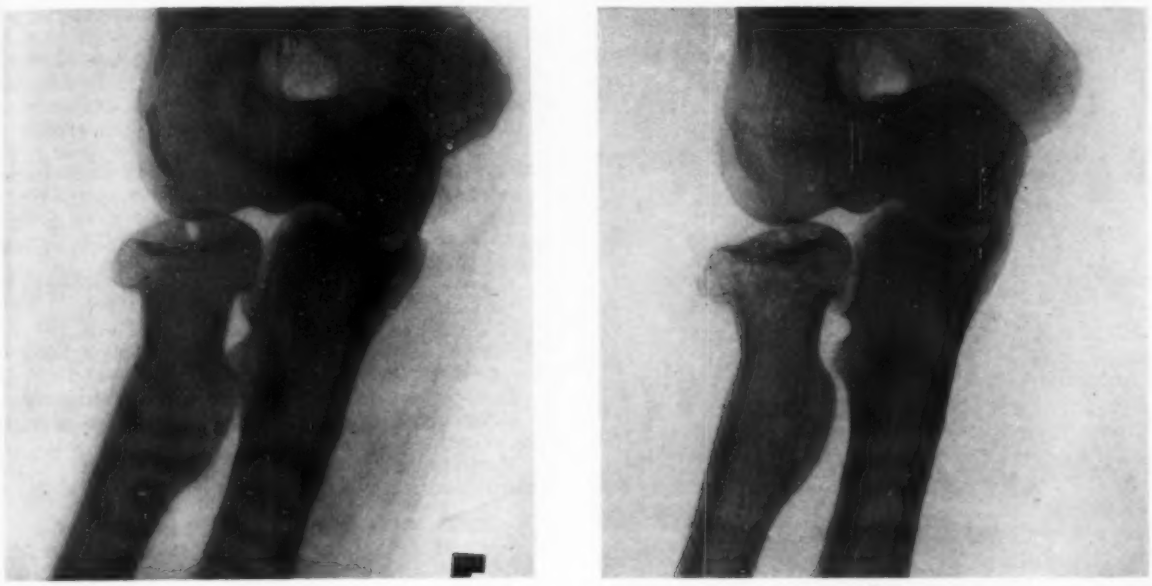
FIG. 153.—*Case* V. C. A, The original anteroposterior X-ray picture of a Type 2 fracture of the radial head. The sector fracture is less than one-quarter of the articular circumference, is depressed below the joint surface, and is not tilted. B, The lateral radiograph taken 15 months later. The plateau of the head of the radius is not distorted and the elbow-joint appears normal. Note the 'chip' fracture of the coronoid process visible in both radiographs. The function of the joint was full.

The 8 'borderline' cases were absent from their work for an average period of 11·5 weeks; but 4 of them had had to undertake work of a lighter nature.

2. *Cases treated by Operation.*—The 5 patients treated by excision of the head of the radius were doing their normal household duties in an average of 8·5 weeks.

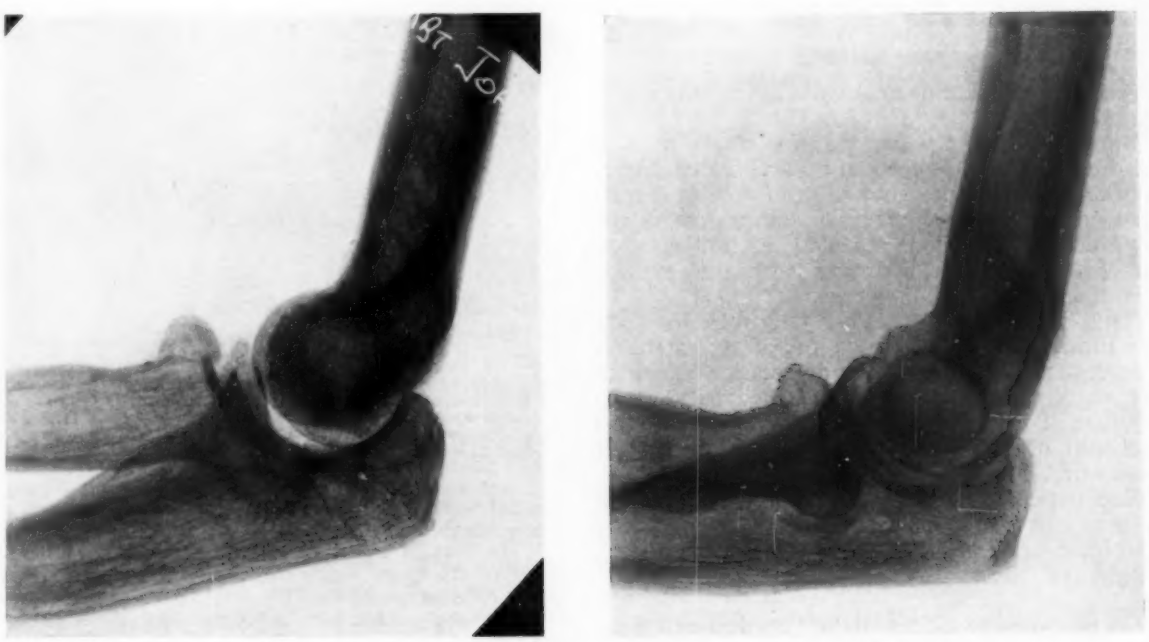
This series of 20 cases of Type 2 fracture of the head of the radius demonstrates some interesting features.

The 7 patients of this group in which the segmental fracture consisting of less than one-quarter



A B

FIG. 154.—*Case* E. W. A, The original anteroposterior radiograph. The fracture of the head of the radius had been considered a 'borderline' case and treated conservatively. The fracture involves more than one-quarter of the articular plateau and it tilted out of line. B, The subsequent radiograph taken 27 months later. The fracture has united, leaving a grossly distorted radial head. Note the fissure still present in the articular plateau. This patient had lost 60° of rotation range of the elbow-joint and was now undertaking lighter work.



A B

FIG. 155.—*Case* R. J. A, Showing the original lateral radiograph of a Type 2 fracture of the head of the radius considered 'borderline' and treated on conservative lines. The fracture involves one-quarter of the articular circumference, but is tilted out of line. B, The subsequent radiograph, taken 42 months later, shows a healed fracture with gross distortion of the articular plateau and early osteo-arthritic changes. This patient, on account of the loss of rotation movement, was forced to give up work involving the use of a shovel.

of the articular circumference of the radial head was depressed below the joint surface without tilting, had all regained full use of the elbow despite an average loss of 10° of extension movement and 30° of total rotation range of the elbow-joint. They

FIG. 156.—*Case* P. S. Anteroposterior radiograph taken 18 months after resection of the radial head for a Type 3 fracture. There is no osteo-arthritis and minimal new-bone formation around the radial neck. Function of the elbow-joint was full.

had returned to their normal work in an average of 5 weeks.

The 5 patients on whom excision of the head of the radius had been performed on account of distortion of the articular plateau, had full function despite the loss of the last 20° extension movement of the elbow-joint. They had regained a full rotation range of movement and had returned to their normal duties in an average of 8·5 weeks.

The 8 ' borderline ' cases had only regained good elbow function with an average loss of 15° extension movement, but with 60° loss of rotation range of elbow movement. They had returned to work in an average of 11·5 weeks, but 4 patients were unable on account of this rotation loss to return to their normal work.

Nine patients of these 20 complained of some pain over the radial head, but no pain over the medial joint ligament.

Eight of these cases were the ' borderline ' cases.

It is proposed to discuss these ' borderline ' cases below.

As with the Type 1 fracture, a constant feature of this series of 20 cases was the loss of extension motion of the elbow-joint even after excision of the radial head.

ANALYSIS OF THE 18 CASES OF TYPE 3 FRACTURE (*Comminuted Fracture involving the Whole Radial Head*)

ORIGINAL TREATMENT.—Each of these 18 cases had been treated by total excision of the radial head. They consisted of cases in which there had been complete disorganization of the head of the radius.

Excision had been carried out on an average of 6 days after the initial injury.

FINDINGS ON CLINICAL EXAMINATION.—

Pain in the Elbow-joint.—Eight patients complained of minimal pain over the lateral joint line, and on rotation of the joint crepitus could be elicited in this area.

Ten patients made no complaint of pain. There was no pain over the medial joint line and no undue laxity in any of them.

No abnormality of the distal radio-ulnar joint was demonstrable in any of these 18 cases. The ' carrying angle ' in each case was normal.

Range of Movement of the Elbow-joint.—None of these 18 patients had a full range of joint movement. In 17 of them extension was limited by an average of 25°. Supination and pronation range was limited by an average of 15° of each movement.

One patient who developed myositis ossificans had an elbow fixed in 90° of flexion. There was minimal range from this position.

Function of the Elbow-joint.—Seventeen of these patients had full use of the joint and were all doing their

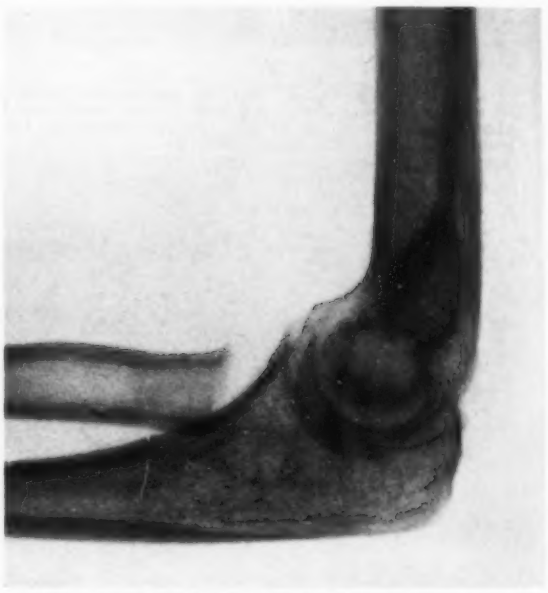


FIG. 157.—*Case* M. B. Lateral radiograph taken 31 months after operative treatment for a Type 3 fracture. The joint surfaces are normal and there is minimal new-bone formation in the region of the radial neck. This patient was doing his normal work as a farm labourer.

normal work. Eight were housewives and 9 were men doing heavy work.

The loss of extension of 25° was no disability and none of the cases had noticed the 30° loss of rotation range of movement.

The one patient with myositis ossificans was coping with her housework, but had a poor function of the joint.

RADIOGRAPHIC EXAMINATION OF THE ELBOW-JOINT.—Eight of the 18 cases were selected at random and subjected to X-ray examination. Typically the radiograph showed complete excision of the radial head. There

was no evidence of degenerative change, and the joint surfaces were normal.

Some new bone had formed in the region of the radial neck, but did not encroach on the new 'joint space'.

Figs. 156 and 157 show the radiographs of two typical cases, taken 18 months and 31 months after resection of the radial head. There is minimal new bone formation and no osteo-arthritis.

TIME OFF WORK.—The average time off work for these 18 cases was 9·5 weeks.

The housewife had returned to her normal duties in 8 weeks, whilst the heavy worker had returned to his in 11 weeks.

This analysis of 18 cases of comminuted fracture of the radial head treated by early excision demonstrates that 17 patients had regained full use of the elbow-joint and were back doing their normal work in 9·5 weeks. This function had been regained despite an average loss of 25° of full extension movement of the elbow-joint. This loss of extension range was no disability. The loss of 30° of rotation range likewise was no hazard to full work. One patient with myositis ossificans had no range of movement of the joint and poor function.

Eight patients complained of occasional pain over the lateral joint line, but it was insufficient to impair the function of the joint.

A constant feature in all these cases despite the absence of the head of the radius was the loss of extension movement of the elbow-joint.

DISCUSSION

Jones (1935) succinctly states that " the fracture of the head of the radius is a serious injury, and whilst the prognosis is good for recovery of a useful elbow, rarely is it a normal elbow ".

This clinical review of 100 cases of all types of fracture of the head of the radius adequately bears out this statement.

Only 1 patient, complicated by myositis ossificans after excision of the radial head, had poor function of the elbow-joint. The remaining 99 patients had all recovered full or good function, and were able to return to their work, although 4 of them had had to undertake work of a lighter nature on account of a residual disability.

The aim of any orthopædic procedure is to attempt to restore normal function whenever possible and as soon as possible.

Method of Treatment and the End-result.—A study of the detailed analysis of the cases of each type of fracture reveals some interesting considerations.

Each of the 62 cases of Type 1 fracture—fissure or marginal sector fractures without displacement—treated by conservative measures, had regained full function of the joint, whilst 42 of these patients having regained a full range of elbow movement, had also recovered a normal elbow. This function had been restored in an average of 4·8 weeks.

This indicates that for the best chance of a perfect result, the fracture of the head of the radius must be in perfect position.

An elbow-joint with full rotation range of movement, but with limitation of flexion and extension is a much more useful member than one in which rotation is limited and the flexion-extension range is full.

The last 40° (one-ninth) of the articular circumference of the radial head plays no part in the rotation movement of the proximal radio-ulnar joint. This review indicates that a loss of 30° range of rotation movement does not adversely affect function. This means in effect that, providing the fracture of the lateral articular circumference of the head involves no more than an arc of 70°, the remaining 290° being intact, the rotation function will be preserved.

From the practical point of view, and despite the theoretical consideration of one-ninth (40°) if more than one-quarter (90°) of the articular circumference of the head of the radius is involved in the fracture, limitation of rotation sufficient to impair function will inevitably result.

Of the 18 cases of Type 3 fracture—comminuted fracture of the whole head treated by resection—17 had regained normal function of the elbow-joint in an average of 9·5 weeks, but none of these had a normal elbow. (The case of myositis ossificans was due to a prolonged unsuccessful search for a fragment of the radial head which was outside the joint capsule.) These 17 patients had recovered almost full rotation, the loss of range being 30°. The loss of extension range of 25° was no disability.

It is considered that this restoration of rotation range was responsible for the ability of these patients to resume their normal duties quickly and efficiently.

The fracture of the radial head without displacement, and the comminuted fracture of the head of the radius, give rise to no difficulty with regard to diagnosis, and there is general agreement on the necessary lines of treatment for each case, i.e., conservative treatment for the non-displaced fracture, and complete excision for the comminuted type of fracture.

The Type 2 fracture—marginal sector fracture with displacement—is unfortunately not so clearly defined.

The analysis of the 20 cases of this type of fracture shows that the 7 patients in whom the sector fracture was less than one-quarter of the circumference of the head, depressed below the joint line, but not tilted in any way, and which were treated conservatively, together with the 5 cases of this group treated by excision of the head on account of gross interference with the radio-humeral joint, had all returned to their normal duties in an average of 5 weeks and 8·5 weeks respectively.

None of these cases had a normal elbow-joint. All had lost full extension of the elbow-joint, but rotation range was full in the 5 resected cases and limited by only 30° in the conservatively treated cases.

Again, it is considered that the regain of full or almost full rotation range was responsible for the relatively early return to a fully-functioning elbow-joint.

The remaining 8 cases of this group labelled 'borderline', constitute a difficult problem. The borderline case, from the practical point of view, is difficult to define.

Most text-books attempt by radiographs to show the maximum displacement of the marginal sector

fracture which is compatible with full function of the elbow-joint if treated conservatively.

The 8 patients of this group were considered in this light, and, as has been shown, none of them

FIG. 158.—The lateral oblique radiograph of a case (not included in this series) in which the anteroposterior and lateral radiographs suggested a 'borderline' case. The segmental fracture appears to consist of one-quarter of the articular circumference of the head, but it is comminuted and tilted out of line. Complete excision of the radial head was performed. *Figs.* 159, 160 show photographs of the radial head after resection.

regained full function mainly on account of the 60° rotation loss of movement. Four of them, because of this loss of rotation, were forced to undertake lighter work. The average time before these 8

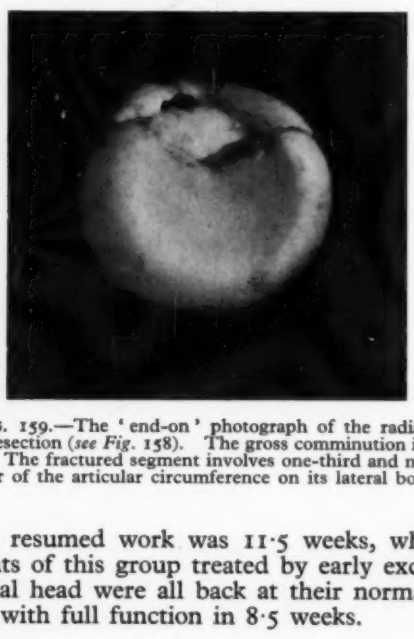


FIG. 159.—The 'end-on' photograph of the radial head after resection (*see Fig.* 158). The gross comminution is easily seen. The fractured segment involves one-third and not one-quarter of the articular circumference on its lateral border.

patients resumed work was 11·5 weeks, whilst the 5 patients of this group treated by early excision of the radial head were all back at their normal occupations with full function in 8·5 weeks.

It would appear, therefore, that unless the fracture is in perfect position, a more certain and quicker return to normal can be secured by early resection of the injured radial head than can be expected by conservative methods.

It is considered that the borderline case should not be regarded as an entity.

If the fracture of the radial head is not displaced, or if the fracture is no more than one-quarter of the articular circumference without comminution, depressed below the joint surface, and not tilted out of line in any way as judged by radiographs in anteroposterior, lateral, and oblique views, conservative measures may be adopted.

In *all* other cases, no matter how minimal the tilting and comminution of the fractured segment, excision of the head of the radius should be performed.

Fig. 158 shows a lateral oblique radiograph of a case (not included in this series) in which the fractured sector appears to consist of one-quarter of the articular circumference of the radial head, with comminution and obvious tilting of the fractured portion. The anteroposterior and lateral radiographs suggested that this was a borderline case. Complete excision of the radial head was performed.

Fig. 159 shows the 'end-on' photograph of the excised head. The fractured segment is grossly comminuted and, in fact, involves *one-third* of the articular circumference and not one-quarter.

Fig. 160 shows the lateral photograph of the excised head. The depression of the fractured sector is well demonstrated. The fracture of the articular circumference, however, is not longitudinal, but on account of the tilting of the fractured portion it is oblique in outline.

This obliquity of the fracture line means that at its base *more* than one-third of the articular circumference of the radial head is involved. Cases, therefore, in which the 'allowable' one-quarter of the articular circumference is damaged, but in which

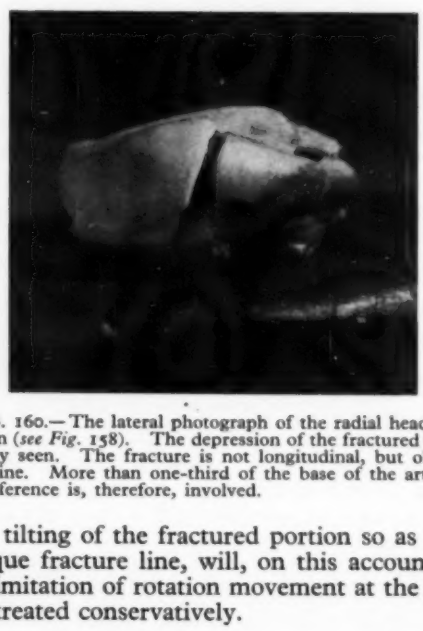


FIG. 160.—The lateral photograph of the radial head after excision (*see Fig.* 158). The depression of the fractured sector is easily seen. The fracture is not longitudinal, but oblique in outline. More than one-third of the base of the articular circumference is, therefore, involved.

there is tilting of the fractured portion so as to give an oblique fracture line, will, on this account, have severe limitation of rotation movement at the elbow-joint if treated conservatively.

This tilting out of line of the fractured sector is a most important factor in deciding the subsequent treatment.

The tightly-fitting pivot proximal radio-ulnar joint needs only minimal mechanical interference to impair its rotation function.

The axiom, I believe, with regard to the treatment of fractures of the head of the radius should be: "If in doubt—resect."

Loss of Extension Range of Movement.—A constant feature in 58 (58 per cent) of these 100 cases was the failure to regain full extension movement of the elbow-joint. The loss of range varied between 8° in the undisplaced fractures to 25° in cases with comminuted fractures. In 23 of these cases complete resection of the radial head had been carried out.

It is the general opinion that the cause of this loss of extension is the damage sustained by the capitellum of the humerus.

It is generally agreed that in the majority of cases the mechanism of injury is such that the capitellum is driven chisel-like into the radial head and that its articular cartilage in consequence suffers damage. This damage is often not apparent at operation, but may develop—in its grossest form as osteochondritis dissecans—at a later date.

The unfortunate patient who attempts to break fall with the hand, the wrist being pronated and dorsiflexed, imparts a tremendous valgus strain on the elbow-joint. At the moment of impact, however, the whole of the elbow-joint sustains a compression force through the long axes of both the forearm bones, and only thereafter, as the elbow sags acutely into valgus, does the radial head bear the brunt of the impact.

The degree of leverage through the radial head and the resultant angle of cubitus valgus determines the degree of displacement and comminution of the head of the radius, and the degree of tearing of the medial joint capsule and ligament.

On impact, however, the cartilage of the trochlea of the humerus and the trochlear notch (greater sigmoid fossa) of the ulna, suffers damage similar to that sustained by the capitellum and the radial head.

The humero-ulnar joint is the 'mainstay' of the elbow. Experimental removal of the head of the radius does not decrease the stability of the elbow-joint, whilst the removal of the olecranon with its trochlear fossa gives rise to a severe degree of laxity. The trochlear notch of the ulna is not perfectly congruent with the trochlea of the humerus, but the joint is nevertheless a tight fit and minimal damage to the cartilage of the joint causes limitation of extension of the elbow-joint.

It was shown earlier in this paper that dislocations of the elbow-joint and fractures of the radial head had a common causative factor.

This factor must, therefore, affect the whole joint and not half of it, and in consequence the cartilage of both the medial and lateral compartments of the joint suffers damage. Only after this has been inflicted, and then depending on the severity of the valgus strain, does bony damage to the radial head occur.

Fig. 153 shows the radiographs of a Type 2 fracture which has completely united. The 'chip' fracture of the coronoid process visible in both the original and subsequent X-ray photographs can only be accounted for by initial damage to both compartments of the elbow-joint.

As has previously been stated, the capitellum and the radial head are not normally in contact. There may be separation of the articular surfaces to an extent of one-quarter of an inch.

For flexion and extension motion to be limited at this joint, a moderately severe mechanical interference is necessary.

A minimal interference with the cartilage of the humero-ulnar joint, however, limits flexion and extension motion.

During the operation for excision of the radial head, examination of that portion of the trochlear fossa of the ulna which can be inspected after the head has been removed often shows evidence of injury in the same way as the capitellum. It may not, however, be immediately apparent, but as with the capitellum, the cartilage may degenerate later.

Twenty-three cases (23 per cent) in this series of 100 patients had incomplete extension of the elbow-joint despite the fact that the radial head, having been completely excised, was not articulating with the capitellum. The damaged capitellum could not, therefore, act as a mechanical bar to this extension movement.

The damage to the trochlea of the humerus and the trochlear notch of the ulna was responsible.

It is considered that the capitellum, whilst certainly responsible for the bony damage to the head of the radius and at the same time suffering damage itself, has innocently been incriminated as the main cause of the loss of extension movement of the elbow-joint after a fracture of the head of the radius.

This loss of movement, in itself no disability, is a result of injury to the whole of the elbow-joint.

Pain in the Elbow-joint.—Pain in the elbow-joint after a fracture of the radial head was not a prominent feature in this series of cases and was never severe.

The interesting feature was that those patients complaining of pain over the medial joint area were patients who sustained fractures without displacement. Pain over the lateral joint area was only observed in patients with either a comminuted fracture of the head, which had been excised, or patients with a partially comminuted fracture, which had not been excised.

It is considered that the medial joint pain is due to the initial tearing sustained by the medial capsular ligament of the elbow-joint during the valgus strain sustained by it. The absence of medial joint pain in the comminuted variety of fractures is due to the dissipation of the abduction force as the radial head collapses, thereby sparing the medial joint ligament.

Pain over the lateral joint line is due to ligamentous damage, especially after resection of the radial head. This minimal pain is often accompanied by crepitus on rotation of the radius. It is of interest to note that this coarse crepitus, often heard and very easily felt, is accounted for by only minimal pathological changes in the articular cartilage when the lateral joint surfaces are inspected.

SUMMARY

1. The surgical anatomy of the elbow-joint, and the mechanism of production of a fracture of the radial head are discussed.

2. A review of 100 cases of fracture of the head of the radius is presented.

3. The end-results are analysed in detail with special reference to the function and range of movement of the elbow-joint, and to the time taken before recovery and return to work.

4. An attempt is made to show that the case which falls on the borderline between conservative and operative treatment should not be regarded as an entity.

5. The axiom in the treatment of fractures of the head of the radius should be: "If in doubt—resect."

6. The cause of the loss of extension movement of the elbow-joint after this type of injury is discussed, and it is considered that the damage to the cartilage of the trochlea of the humerus and the trochlear notch of the ulna, shares a great deal of the responsibility for this loss of range.

7. The cause of pain in the elbow-joint after a fracture of the radial head is discussed.

I wish to thank Mr. R. C. Baird for his constant encouragement. I am indebted to my father, Mr. R. Mason, for the photographs and the radiographic reproductions, and to Mrs. Pamela Carpenter, clinical secretary, for her invaluable help.

REFERENCES

CUTLER, C. W. (1926), *Ann. Surg.*, **83**, 267.
FLEMMING, C. W. (1932), *Proc. R. Soc. Med.*, **25**, 1011.
JONES, S. G. (1935), *New Engl. J. Med.*, **212**, 914.
KEY, A. J. (1931), *J. Amer. med. Ass.*, **96**, 101.
MASON, M. L. (1953), *Brit. J. Surg.*, **60**, 340.
MURRAY, R. C. (1940), *Ibid.*, **28**, 106.

THE ANATOMY OF THE INTRARENAL ARTERIES AND ITS APPLICATION TO SEGMENTAL RESECTION OF THE KIDNEY

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PARTIAL nephrectomy is now advocated by many surgeons in the treatment of renal tuberculosis and calculus. Control of hæmorrhage is one of the technical difficulties of this operation and of the more established procedure of nephrolithotomy in which failure of hæmostasis sometimes necessitates nephrectomy. Knowledge of the vascular pattern of the kidney should assist the surgeon in carrying out these operations, but it is neither complete nor readily accessible. This investigation was, therefore, carried out to answer the following questions:—

1. Is there a constant pattern of the branches of the renal artery within the substance of the kidney?

2. If the pattern is constant, is there a collateral circulation between these branches?

3. Could knowledge of the two previous points be applied to segmental resection of the kidney?

4. In view of the density of the kidney substance, apart from anatomical knowledge, is there any method of determining the pattern and course of the intrarenal arteries either before or at the time of operation?

METHODS OF INVESTIGATION

The investigation was carried out by two methods:—

Injection of Post-mortem Specimens with Plastic.—The kidney and the surrounding tissue were removed *en bloc* with the adjacent part of the aorta. This was done so that any duplication of the renal vessels might be detected and examined. Liquid polyester resin (Marco Resin S.B. 61C) was injected into the renal artery and subsequently, when the resin had set, the kidney substance was removed by corrosion in concentrated hydrochloric acid. Casts were made of the renal vessels of more than thirty specimens.

Angiography of Post-mortem Specimens.—Post-mortem kidneys were perfused at a pressure approximating to that which they had received in life. Angiograms were made by injection of 50 per cent and 70 per cent solutions of diodone into the renal artery. Similarly, venograms were made by perfusion of the renal veins.

ANATOMY AND NOMENCLATURE

On the basis of the arterial distribution, the kidney is divisible into five segments (*Fig.* 161). From above downwards these are:—

The Apical Segment is a cap of tissue which occupies the medial side of the upper pole of the kidney, mainly on its anterior surface.

The Upper (*Anterior*) *Segment* lies in the anterior plane of the kidney. It covers an area which includes the upper pole and part of the central area of the kidney.

The Middle (*Anterior*) *Segment* lies in the anterior plane of the kidney. It covers an area in the lower central part, between the upper and lower segments.

The Lower Segment forms the lower pole of the kidney. Unlike the middle and upper segments, it lies in both the anterior and posterior planes of the kidney.

The Posterior Segment lies entirely in the posterior plane of the kidney and occupies an area between the posterior part of the apical segment above, and the posterior portion of the lower segment below.

ANATOMY OF THE RENAL VESSELS WITHIN THE KIDNEY

Each segment is supplied by its own artery (*Figs.* 162, 163). The main stem of the renal artery divides at a variable point between the aorta and the

hilum of the kidney into an anterior and posterior division.

The *anterior division* gives rise to the upper, middle, and lower segmental arteries, and the apical segment artery usually arises from it.

The *posterior division* continues and supplies only the posterior segment, but it may give origin to the artery to the apical segment.

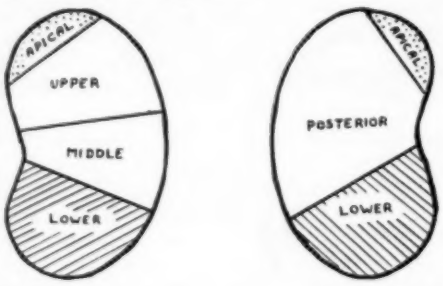

FIG. 161.—A diagram of the left kidney showing the segments which are based on the arterial distribution. Only the apical and lower segments occupy areas on both the anterior and posterior surfaces of the kidney.

whose origin is the most varied of all the segmental arteries. In order of frequency, it arises from the short trunk of the anterior division or the upper

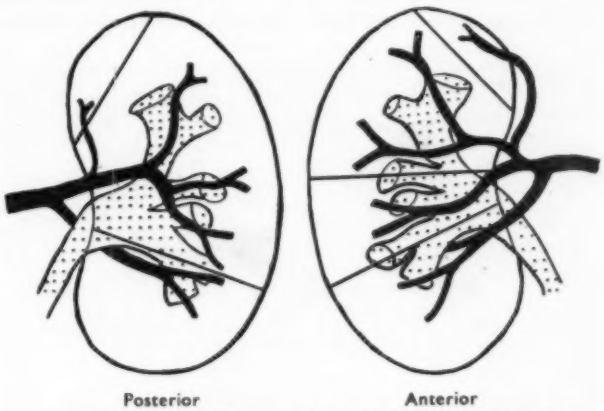

FIG. 162.—A diagram of the right kidney showing the arrangement of the arteries and the segments they supply. The artery to the apical segment is that of *Type I*. The arrangement of the remaining anterior segment arteries is that of Group I.

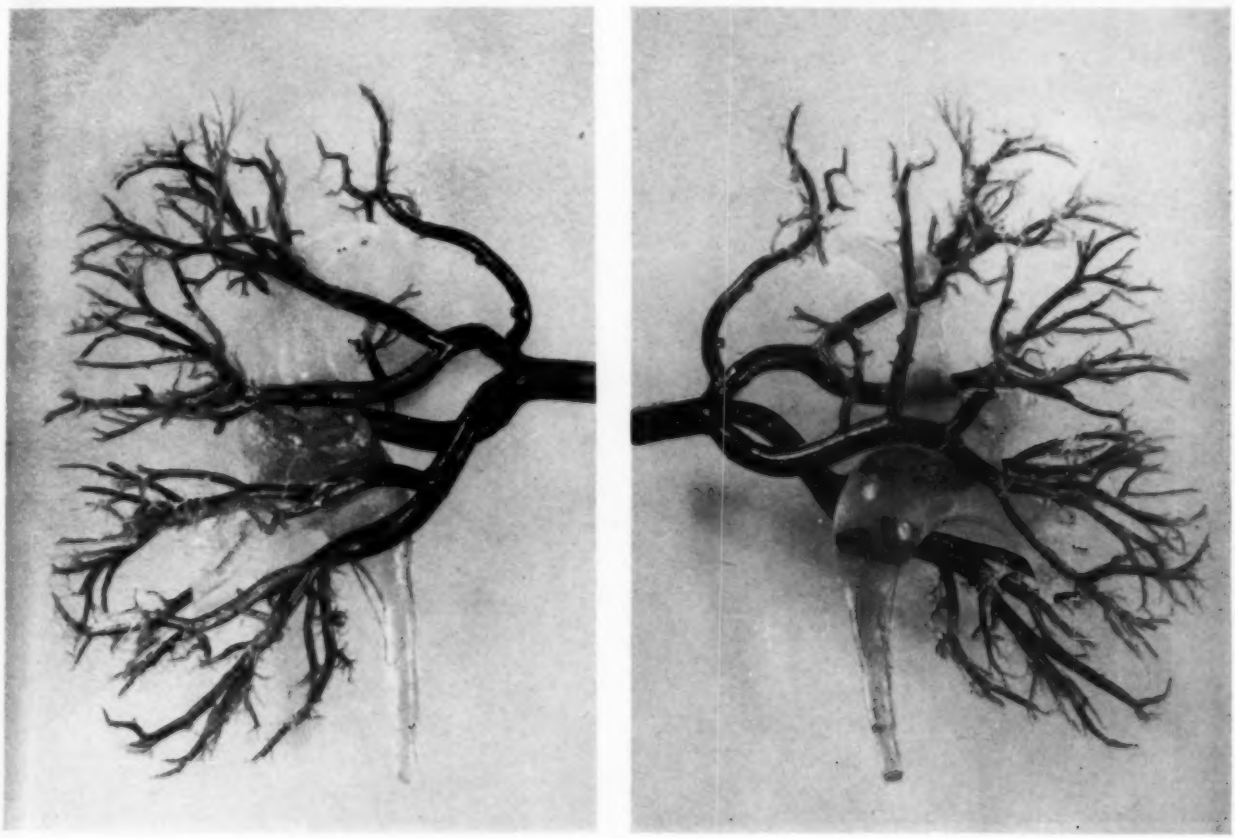

FIG. 163.—A cast of the intrarenal arteries of the right kidney. A, *Anterior view*, The apical segment artery arises from the artery to the upper segment, the apical and lateral branches of the latter being well developed. The middle segment artery arises from the side of the lower segment artery, as in Group II. B, *Posterior view*, The artery to the posterior segment lies close to the superior pelvi-calicine junction; it gives rise to upper, middle, and terminal branches. Note the posterior branch of the lower segment artery from the anterior division.

The Segmental Arteries.—

The Apical Segment Artery.—The apical segment is supplied by an artery which most frequently arises from the anterior division. It is, however, a vessel segment artery; from the junction of the anterior and posterior divisions with the main stems; from the main stem or the aorta; from the posterior division (*see Fig.* 164).

Type I: In 43·3 per cent of cases the artery arises from the trunk of the anterior division or the artery to the upper segment. If it arises from the anterior division its point of origin is easily seen in the hilum well away from the solid substance of the kidney. If it arises as a branch of the upper segment artery its point of origin may be seen in the hilum, under the lip of the hilum, or more rarely within the parenchyma.

Type III: In 23·3 per cent of cases the artery arises from the main stem or the aorta itself. The artery runs with its fellow to the hilum, or it may make an extrahilar entry into the side of its segment and in this respect may have the appearance of an 'aberrant' or 'accessory' artery. In this series of specimens, about one-third of this type had an extrahilar entry, most of the vessels having arisen directly from the aorta.

FIG. 164.—A diagram of the variations of origin of the artery to the apical segment in a right kidney. *Type I*, It arises from the upper segment artery. *Type II*, It arises from the junction of the anterior and posterior divisions with the main-stem artery. *Type III*, It arises near the aorta and makes an extrahilar entry to its segment. There is a small accessory artery to the segment arising from the posterior division. *Type IV*, It arises from the posterior division.

FIG. 165.—A, The cast of the lower segment which has become separated from the rest of the cast of the kidney, whilst in the acid bath. B, The separated segment, after being replaced in the main cast.

Type II: In 23·3 per cent of cases the artery arises from the junction of the anterior and posterior divisions with the main stem. This point of origin is either in the hilum or nearer the aorta. The vessel enters its segment usually from the anterior aspect of the hilum.

Type IV: In 10 per cent of cases the artery arises from the posterior division and enters the segment from the posterior aspect of the hilum.

Accessory Apical Segment Artery.—In one-third of the specimens there is a small accessory artery to the apical segment which frequently originates from

the posterior division and enters the segment from that aspect. Accessory vessels are present mainly in two types of cases: In those where the main artery enters the segment 'high up', that is, an extrahilar entry, and thereby leaves a small area between the point of entry and the base of the segment which is supplied by the accessory vessel. In those cases where both the artery to the upper segment and the artery to the apical segment lie nearer the lateral border of the kidney, a small area is left on the posteromedial side which is supplied by the accessory vessel (*Fig.* 164, *Type III*).

The Upper Segment Artery.—It arises from the anterior division and enters the segment at its base. Its point of origin is usually in the hilum, or under the hilar lip, and can be easily seen. Soon after its entry into the segment it divides usually into two branches: an apical branch which runs upwards and lies in front of the upper calix; a lateral branch which runs laterally to supply the lateral border of the kidney. The presence and size of these two branches depends largely upon the size and shape of the upper calix. If the pelvi-caliceal system is long and narrow both branches are well formed (*see Fig.* 169), but where there are only small middle calices or the artery to the middle segment is big, then the lateral branch is usually small.

The Middle Segment Artery.—It arises from the anterior division. If the middle calices are present it supplies the kidney substance on their anterior aspect, its terminal branches interdigitating with those from the posterior division. If the upper and lower major calices are large, and there are no middle calices, then the middle segment and its artery are correspondingly small, the latter supplying the 'gap' between the two major calices.

The Lower Segment Artery.—This artery arises from the anterior division. It passes usually in front of the pelvis or ureter and soon after its entry into the segment it divides into an anterior and posterior branch. The presence and course of these two branches is so constant that the lower pole of a cast or an arteriogram can always be recognized by it. The anterior branch divides and supplies the anterior aspect of the lower calix and the tip of the lower pole. The posterior branch passes under the neck of the lower calix and supplies the posterior and lower aspect of the lower pole.

The Posterior Segment Artery.—This is the continuation of the posterior division. It enters the posterior aspect of the hilum, running from front to back across the upper border of the pelvis of the kidney. It then passes behind and in close association with the junction of the upper calix and the pelvis; this relationship is a constant landmark. The artery runs under the lip of the hilum and forms a curve (Albarran, 1909) from whose lateral border branches radiate outwards and enter the segment. The branches form three groups: an upper group of one or two in number which supplies the posterior part of the upper calix; if there is one vessel only, it is often large. A middle group, which is usually small and interdigitates with those of the middle segment from the anterior division. The terminal group, branches of which supply the upper part of the lower calix on its posterior surface, the area being larger when the posterior branch of the lower segment artery is small.

The Nature of the Arterial Supply.—This investigation has shown that there is no collateral arterial blood-supply between the segments. This

FIG. 166.—A cast of the right kidney (Group III) in which the artery to the middle segment was ligated before injection. The cast shows a 'bare area' corresponding to that of the segment.

fact has been proved in four ways: In those cases where a segmental artery took its origin from the aorta the vessels were injected separately. When the cast was taken from the corrosive acid bath a complete cast of the segment, together with its artery was often found lying free in the acid, it having fallen apart from the main cast when the supporting organic tissue of the kidney had been removed by the acid. The separated segment, when replaced in the main cast, fitted snugly like a piece in a jig-saw puzzle (*Fig.* 165).

Injection of individual segments with different coloured resins showed no transgression of colour from segment to segment.

If a segmental artery was ligated before injection of resin into the main stem was done, a 'bare area' was found in the cast corresponding to that of the segment excluded by the ligated artery (*Fig.* 166).

Segmental arteriograms were made and it was found that diodone did not pass from one segment to another and that each segment could be excluded by compression of its segmental artery (*see Fig.* 167).

The Intrarenal Venous System.—There is a free anastomosis of the intrarenal veins, which do

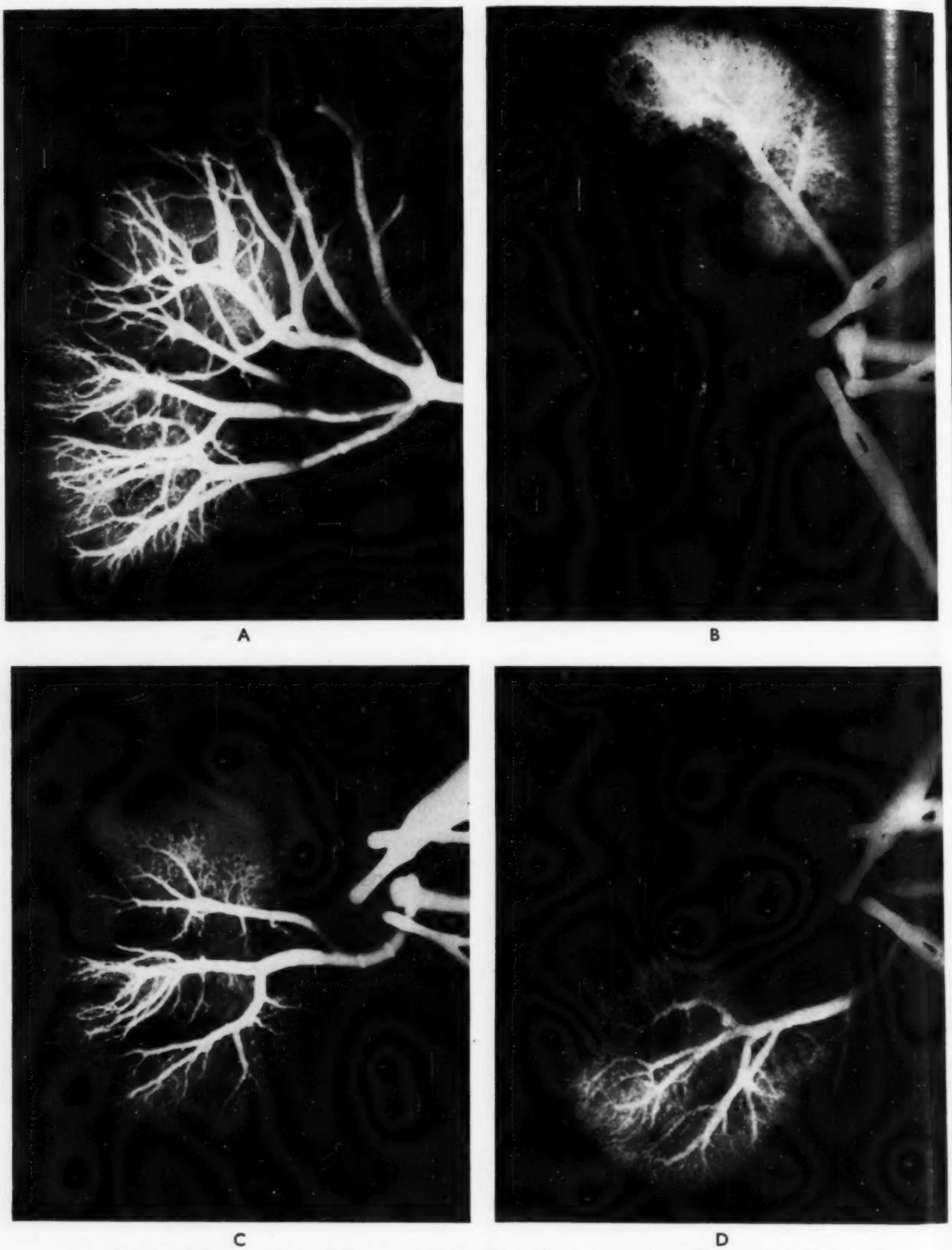

FIG. 167.—An arteriogram of the same kidney as seen in *Fig.* 166. A, A complete arteriogram of all branches of both anterior and posterior divisions. B, Arteriogram of the apical segment. The remaining segmental vessels have been occluded by clamps. C, Arteriogram of the middle segment; compare this with (A) and also the 'bare area' in *Fig.* 166. D, Arteriogram of the lower segment; compare this with (A) and also *Fig.* 166.

not follow a segmental arrangement as do the arteries. The presence of a free venous anastomosis was noted by Lee Brown (1924) and has been confirmed in this investigation by three findings: Examination of a cast made of the venous system within the kidney shows the anastomosis to be free; perfusion of one renal vein resulted in an equivalent flow from the other vein; a perfusion venogram confirmed the same fact.

VARIATIONS IN THE ARTERIAL PATTERN

In this series of casts the presence of individual segmental arteries has been constant. The only variation has been one of size (usually related to the variation in the size of the segment concerned) and of the exact point of origin of the artery from the main stem.

Variations in the Origins of the Segmental Arteries.—The main stem artery divides into an anterior and a posterior division at any point between the aorta and the hilum. The posterior division continues as the artery to the posterior segment and has no further variation in its course or origin.

The variations in the origin of the artery to the apical segment have been described. It is with the remaining segmental arteries, the upper, middle, and lower arteries of the anterior division that variations of origin occur. These variations fall into three groups (*Fig.* 168).

Group I: The lower artery arises first; the upper and middle arteries have a common origin. The artery to the lower segment may originate at any point between the hilum and the aorta or it may arise separately from the aorta a little below the origin of the main stem. This group is the most common, it occurs in 53·3 per cent of cases (*see Fig.* 169).

Group II: The lower artery arises with, or more usually a little proximal to, the upper artery. The middle artery arises from the side of the lower artery. This is the next most common group, occurring in 30 per cent of cases (*see Fig.* 163).

Group III: The lower, middle, and upper segmental arteries have their origin at a common point. This group occurs in 16·6 per cent of cases (*see Fig.* 170).

DISCUSSION

This investigation has yielded a number of facts about the renal vascular pattern which have practical applications in segmental or partial resection of the kidney.

The distribution of the arteries within the kidney forms a pattern which is constant, and upon this is founded the division of the renal parenchyma into five segments.

There is no collateral arterial supply between these segments. Ligation of a segmental artery will not produce ischæmia nor interference with the blood-supply of the neighbouring segments. This lack of arterial anastomosis will render the technique of resection easier since the field of operation will be relatively bloodless following the ligation of the segmental artery. This is borne out by Eberhart and Banks (1952), who found that ligation of the artery supplying the area of operation produced an almost bloodless operating field. Lastly, the origins of the segmental arteries are accessible. In the majority of cases they are easily seen in the hilum and often at points nearer the aorta. This is of value, since segmental resection is most frequently carried out from the hilum towards the periphery.

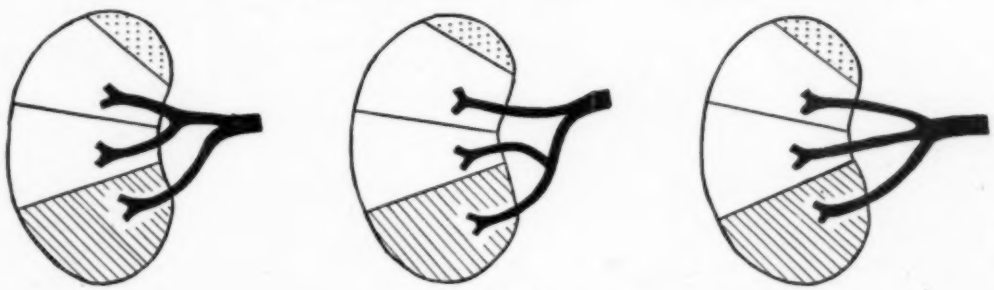

FIG. 168.—A diagram of the right kidney showing the variation in origin of the upper, middle, and lower segment arteries from the anterior division.

Most of the variations so far encountered have fallen easily into the groups which have been described, and if at operation dissection is carried from the aorta towards the hilum, the segmental vessels can be identified as they originate from the main stem. Knowledge of the variations in the origins of these segmental arteries is important in segmental resection, and no vessel should be ligated until its distribution has been confirmed. For example, it is important to distinguish between Group I and Group II, since ligation of the lower segment artery near its origin would only affect the lower segment in Group I but would leave the middle segment ischæmic in Group II. In the latter group ligation of the lower segment artery must be made after it has given origin to the middle segment artery, unless it is proposed to remove both middle and lower segments.

At operation, temporary compression of a vessel results in a purplish discoloration of the area supplied, and enables the amount of tissue for resection to be determined (Abeshouse and Lerman, 1950).

The arrangement of the renal arterial segments is such that only resection of the upper or lower pole is of practical value, since on anatomical grounds alone, apart from those of pathology, the single resection of say the middle or posterior segment

would be both impracticable and useless. In practice, the nature of the pathology may necessitate that the site of resection be determined more on the arrangement of the calicine than the arterial pattern, and this may call for resection of a segment with an additional subsegment. Abeshouse and Lerman (1950) have recorded both personal and collected cases of partial nephrectomy of the upper or lower pole for stone. Of these, there were 107 cases in which the lower pole was removed and 56 cases in which the upper pole was removed; they record that the midportion of the kidney (middle calix) was removed in 8 cases. More recently, Eberhart and Banks (1952) have recorded 15 personal cases in which removal of the upper pole was done in 11 cases and removal of the lower pole in 4 cases. Twinem (1940) found that calculus is more than twice as common in the inferior calix than in the upper calix. This is likely to account for the predominance of operation for the removal of the lower pole, rather than the fact that removal of the lower pole is the easier operation.

Resection of the lower pole involves removal of the lower segment, for which the segmental artery is ligated and the plane of section of the parenchyma is carried radially from the hilum on a line between the middle and lower segments in the anterior plane, and between the posterior and lower segments in the posterior plane. When resection of a major calix, to prevent recurrent stone formation (Hamilton Stewart, 1952), is done, it may be necessary to resect a larger area of the parenchyma and to remove the middle and part of the posterior segments in addition to the lower segment.

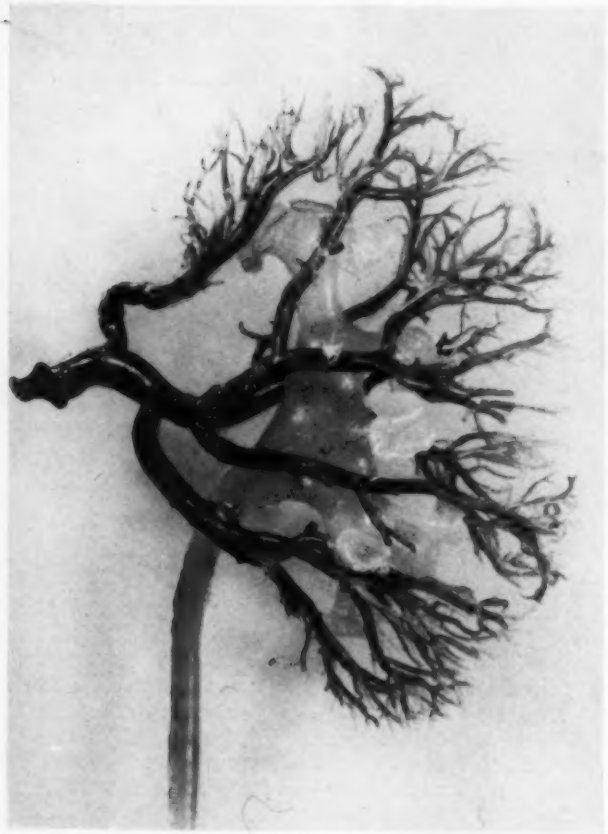

FIG. 169.—A cast of the left kidney. The apical segment artery arises from the anterior division. The origins of the remaining anterior segment arteries are as in Group I.

FIG. 170.—A cast of the right kidney. The origins of the anterior segment arteries are as in Group III. The apical and lateral branches of the upper segment artery are well developed. The apical segment artery arises from the posterior division.

Resection of the upper pole will involve removal of the apical segment, and since this usually contains such a small portion of the upper calix, it will be necessary to remove subsegments of the upper and posterior segments. The line of incision radiates from the hilum, and in addition to ligation of vessels in the hilum it will be necessary to ligate some arteries within the kidney substance, for example the apical branch of the artery to the upper segment, where the incision cannot conveniently be made parallel to them. Ligation of the vessels within the renal parenchyma can be done by the method described by Eberhart and Banks (1952), who place a stitch in the parenchyma around the blood-vessel so that when tied the ligature cuts through the soft tissue until the noose contains only the vessel. It is important that the line of incision be carried above the curve of the artery to the posterior segment, where it lies close to the superior pelvi-calicine junction, since damage to the artery here will produce necrosis of the remainder of the posterior segment.

Abeshouse and Lerman (1950) state that the operative mortality for partial nephrectomy is low, 2·58 per cent, compared with that of nephrolithotomy, which is 6·3 per cent. There is a correspondingly low morbidity rate, the incidence of secondary hæmorrhage, persistent urinary fistula, and recurrent stone formation being lower after partial nephrectomy than after nephrolithotomy. Hamilton Stewart (1952) and Eberhart and Banks (1952) also advocate partial nephrectomy in preference to nephrolithotomy. Although these facts suggest that partial nephrectomy is the operation of choice for calculus in the upper or lower calices, most of these authors agree that there is still a limited place for nephrolithotomy.

For nephrolithotomy, Brodel (1901) advocated an incision on the posterior side of the lateral border of the kidney. Examination of this series of casts has shown that this is by no means a bloodless area, and it is suggested that if the incision is made on a radial and intersegmental plane, at any rate in the lower pole of the kidney, it may prove to be less vascular both at the time of operation and in the post-operative period.

Study of this series of casts has shown that if the arteries of the renal pedicle are examined in conjunction with those in the kidney substance, and not as a separate entity, as is so often the case in anatomical and surgical teaching, then it becomes clear that many of the so-called 'aberrant' or 'accessory' arteries are not so, but are merely normal segmental vessels with a precocious origin. Gerard (1911), in his study of 150 pairs of kidneys, was probably the first to recognize that the presence of additional vessels at the hilum was due to an early division of the main renal artery, rather than a true multiplication of arteries. This concept is important in the planning of a segmental resection, since ligation of a vessel on the grounds that it is an accessory artery will lead to necrosis of a segment or part of a segment.

A number of authors have recorded that in cases where additional arteries are present, those to the lower pole are most frequent. Weinstein, Countiss, and Derbes (1940) found that the incidence of accessory vessels passing from the aorta to the lower pole was approximately twice that of those going to the upper pole. The same fact is recorded by Albarran (1909). In this series it has been found that in 63 per cent of casts the lower segmental artery has the most proximal origin of the three segmental arteries in the anterior division. This tendency of the lower segmental artery to have its origin from, or nearest, the aorta is probably related to the fact that the arteries of the causal embryological segments which supply the mesonephros retain their individual origin from the aorta, whereas those at the cephalic end tend to coalesce (Felix, 1912). It is suggested that the name 'aberrant' should be reserved for those arteries whose course is truly abnormal and whose origin is from a vessel other than the aorta, as for instance, those arising from the superior mesenteric or spermatic vessels, as described by Anson, Cauldwell, Pick, and Beaton (1948).

In some cases the main-stem artery does not divide until it reaches the hilum, and at operation identification of some of the segmental arteries may be difficult. Arteriography of the intrarenal arteries will make identification possible, and also when identification of a segmental vessel has already been made at operation, a segmental arteriogram (*see Fig.* 157) will be of confirmatory value. It would be a help to have a pre-operative renal arteriogram, and the same procedure will give an excretory pyelogram (Goodwin, Scardino, and Scott, 1950). An arteriogram done at the time of operation, however, would be of value.

SUMMARY

1. The study of plastic casts and of arteriograms of the human intrarenal arteries has shown that there is a segmental arrangement of these vessels which is constant, and that there is no collateral arterial circulation between these segments.

2. On the basis of the arterial distribution the renal parenchyma is divided into five segments—the apical, upper, middle, lower, and posterior—each of which is supplied by its own artery.

3. Many of the so-called 'aberrant' and 'accessory' arteries are normal segmental vessels with a precocious origin.

4. Knowledge of the segmental distribution of the arteries is of value in the bloodless approach to nephrolithotomy and in segmental resection of the kidney.

I wish to thank Professor R. S. Pilcher, who gave me much kindly help and advice, and also the opportunity to carry out this work.

I am grateful to Mr. Bentley Purchase, Dr. F. Camps, and Dr. R. A. Drury for giving me access to post-mortem material, and to Dr. E. G. Redman for advice on radiographic technique.

REFERENCES

ABESHOUSE, B. S., and LERMAN, S. (1950), *Surg. Gynec. Obstet.*, **91**, 209.

ALBARRAN, J. (1909), *Médecine operatoire des Voies urinaires*, 42. Paris: Masson.

ANSON, B. J., CAULDWELL, E. W., PICK, J. W., and BEATON, L. E. (1948), *J. Urol.*, **60**, 732.

BRODEL, M. (1901), *Bull. Johns Hopk. Hosp.*, **12**, 13.

BROWN, R. K. LEE (1924), *Arch. Surg., Chicago*, **8**, 842.

EBERHART, C. A., and BANKS, R. (1952), *Amer. Surg.*, **18**, 684.

FELIX, W. (1912), *Human Embryology* (ed. Keibel and Mall), Vol. 2, Fig. 572 and p. 822. Philadelphia: Lippincott.

GERARD, G. (1911), *J. Anat., Paris*, **47**, 531.

GOODWIN, W. E., SCARDINO, P. L., and SCOTT, W. W. (1950), *Ann. Surg.*, **132**, 944.

STEWART, H. HAMILTON (1952), *Ann. R. Coll. Surg. Engl.*, **11**, 37.

TWINEM, F. P. (1940), *J. Urol.*, **44**, 599.

WEINSTEIN, B. B., COUNTISS, E. H., and DERBES, V. J. (1940), *Urol. cutan. Rev.*, **44**, 137.

HYPERPARATHYROIDISM DUE TO PARATHYROID ADENOMA

REPORT OF SIX CASES AND A REVIEW

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THE condition of generalized osteitis fibrosa cystica was first reported by Von Recklinghausen in 1891. The association of this osteodystrophy with a parathyroid tumour was described by Askanazy in 1903. However, the first operation for this condition was not performed until 1926, when Mandl removed a tumour from a patient suffering from hyperparathyroidism. Hunter and Turnbull's classical paper in 1931 confirmed the coexistence of parathyroid tumours and bone disease and demonstrated the regression of symptoms following the extirpation of the tumour. Albright (Albright and Reifenstein, 1948) has recently stressed that skeletal disease is only part of the clinical syndrome of hyperparathyroidism and many patients with this disorder maintain a positive calcium balance and show no clinical or radiological evidence of bone disease.

The fully developed osteitis fibrosa cystica presents little difficulty in diagnosis. In early hyperparathyroidism a solitary bone cyst, myeloid tumour, or myeloid epulis may be treated as such, and the true nature of the underlying disease may pass unrecognized (*Case* 3). Severe bone pain without accompanying clinical signs may be thought to be 'functional' or due to 'arthritis' or neuritis (*Cases* 2 and 5). The polyuria which results from hypercalcuria may simulate diabetes and its real significance escape unobserved (*Case* 5). Barney (1936) found that 3 per cent of all patients with renal calculi suffered from hyperparathyroidism, and many such patients are not diagnosed until an osteodystrophy develops (*Case* 1).

The present series of 6 cases is illustrative of the difficulty in early diagnosis. It is felt that a full biochemical investigation, including serum-calcium, inorganic phosphorus, alkaline phosphatase, and calcium balance (Albright and Reifenstein, 1948), will lead to a diagnosis of hyperparathyroidism in a small but definite percentage of patients with bone pain, renal calculi, or isolated bony lesions. Sulkowitch's test is always positive in hypercalcuria and provides a useful urine test to indicate which cases are suitable for further investigation.

CASE REPORTS

Case 1.—The following case of parathyroid adenoma was associated with severe bony changes in the thorax and spine and terminated in renal failure. An interesting coincident finding was a carcinoma of the stomach. The occurrence of the latter condition caused clinical suspicion of bony metastases.

Mrs. K., aged 64, was admitted on April 1, 1952, with a history of one year's gradual loss of weight, anorexia, and increasing lassitude. She had become a travesty of her previous stature in a short period owing to an increasing kyphosis. Six years previously she had a gastrectomy for carcinoma of the stomach, which histological examination showed to be an anaplastic adenocarcinoma. A good recovery followed the gastrectomy and her appetite and weight returned to normal. This improvement was maintained until the onset of the present illness twelve months prior to admission.

ON EXAMINATION.—She was found to be a grossly emaciated elderly woman who complained of generalized pains on the slightest movement in bed. The skin was dry and wrinkled and uniformly pigmented brown. The most striking feature was the gross deformity of the thorax, which consisted of marked rounded kyphosis and prominent sternum similar to a pigeon chest. There was no deformity of the long bones and no enlarged glands in the neck. The liver was not palpable and no definite mass was detected in the abdomen. Radiographs of the vertebræ showed a gross kyphoscoliosis with 'fish-tail' appearance of most of the vertebræ. There was a diffuse mottling of the skull with areas of increased translucency but no platybasia. The pelvis showed deformity with marked porosis, thinning, and distortion of trabecular pattern. A radiograph of the chest showed no evidence of secondary deposits, but fractures of the ribs were seen; a radiograph of the abdomen showed a large renal calculus in the right kidney. The appearances of the skull were thought to be either Paget's disease or hyperparathyroidism; those of the spine and pelvis were almost diagnostic of the latter. There was no indication of secondary deposits in any of the radiographs. The blood-count was normal and the bone-marrow showed no carcinoma cells. The blood chemistry showed a persistently high serum-calcium (12·2 mg. per cent) and alkaline phosphatase (56 K.A. units), and a low inorganic phosphorus (2·2 mg. per cent).

The patient gradually deteriorated from renal failure, the blood-urea rising to 124 mg. per cent, and she died on April 18, 1952.

AT AUTOPSY.—There was a large parathyroid adenoma situated in the left lateral lobe of the thyroid gland. The tumour measured $4\frac{1}{2} \times 2 \times 3\frac{1}{2}$ cm., and weighed 16 g., and was greyish-brown in colour. The cells in the parathyroid tumour were cuboidal in shape with an eosinophil cytoplasm, and round, deeply staining nuclei, and were either arranged in trabeculæ or compact masses. Occasional colloidal material or areas of hæmorrhage were seen between the cells. The right kidney showed pyelonephritis and a large calculus, and the left kidney showed some degree of tubular calcification but was otherwise normal. The stomach showed an adenocarcinoma which had infiltrated through the wall and invaded lymphatics on the peritoneal surface, but the liver was not involved and there were no distant metastases. The histological picture of the bones was characteristic of hyperparathyroidism, with widening of the Haversian canals and the cancellous spaces and replacement of the normal intertrabecular fat by young cellular vascular granulation tissue. The bony trabeculæ were thinned out and had very irregular outlines.

Case 2.—Mrs. W., aged 54, presented with symptoms of 'arthritis' for many years, and a 'bone cyst' had been removed from her clavicle three years previously. The significance of these features was unrecognized until the full osteodystrophy developed.

HISTORY.—For twenty years this patient had complained of 'arthritis'. On various occasions radiant heat had been prescribed without lasting benefit. In 1948 a tumour of the right clavicle was removed at another hospital. In June, 1952, a 'cyst' in the left mandible

was treated elsewhere with radiotherapy. In August, 1952, she was treated at a Psychiatric Centre as a case of reactive depression.

She was admitted to the Royal Infirmary, Sheffield, under the care of Dr. H. P. Brody in February, 1953. At this time she was complaining of polyuria. This symptom had been present for several months and she frequently micturated on six or more occasions during a night. Nausea was almost continuously present and there was occasional vomiting after food. She lacked energy and felt generally unwell. She complained of severe pain in the right shoulder, chest, and right hip and thigh.

CLINICAL EXAMINATION.—A co-operative intelligent patient who walked with obvious pain and difficulty. A painful swelling was palpated over the right scapula, and another of the third right rib at its junction with the costal cartilage. Flexion, abduction, and external rotation of the right hip were limited and painful.

In the light of the subsequent biochemical investigation the neck was carefully palpated, but no nodular swellings were palpable.

BIOCHEMICAL INVESTIGATIONS.—

Serum-calcium (March 23), 14·3 mg./100 ml.

Serum inorganic phosphorus (March 23), 2·1 mg./100 ml.

Serum alkaline phosphatase (March 23), 98 K.A. units.

Urine inorganic phosphorus, 1·08 g./24 hours.

Urine calcium (on restricted calcium intake), 0·378 g./24 hours.

Blood-urea, 33 mg./100 ml.

Urea-clearance, 76 per cent and 76 per cent of average normal.

RADIOLOGICAL INVESTIGATIONS.—

Thorax and Chest: There is a cystic osteoporotic trabeculated lesion in the outer extremity of the right clavicle. Small localized expanding cystic trabeculated lesions in the 2nd, 7th, and 8th left ribs. A similar lesion in the 9th left rib is the site of a pathological fracture (*Fig.* 171).

Pelvis: Generalized bone porosis. A cystic trabeculated porotic lesion in the left superior pubic ramus. There is a small oval area of translucency in the right femoral shaft.

Hands: Showed subperiosteal bone resorption.

Skull: Generalized fine pin-point stippling of the vault with some porosis.

Teeth: The lamina dura is very faintly outlined but is discernible.

A diagnosis of hyperparathyroidism was made and it was decided to explore the neck surgically.

AT OPERATION (B. C. Rowlands, March 24).—No adenomata were found in the normal position. Search posterior to the thyroid fascia was similarly negative. A large, well-encapsulated adenoma was found deep in the posterior superior mediastinum well behind the sternum. It was easily removed.

HISTOLOGICAL REPORT ON THE SPECIMEN.—The specimen consists of a parathyroid gland 4·5 × 3 × 1 cm. and weighing 6·7 g.

Section through the specimen shows the structure of a benign parathyroid adenoma. The clear and eosinophil granular cells are easily distinguishable. They are arranged in cords separated by thin fibrous tissue septa. Numerous dilated sinusoidal capillaries are also to be seen.

SUBSEQUENT PROGRESS.—As in *Case* 5, immediate cessation of bone pain occurred following operation. As anticipated by the high pre-operative serum alkaline phosphatase, a rapid fall in the blood-calcium occurred, accompanied by tetany (*Fig.* 172). Oliguria was also a notable feature (*Fig.* 173). These effects were dealt with by intravenous saline infusion, calcium gluconate being added to the infusion fluid. Infusion was carried out for 48 hours, resulting in a resumption of normal urinary excretion. Sixty c.c. of 10 per cent calcium gluconate was administered daily during two days following onset of tetany and was adequate in controlling it. For the next ten days, twice daily intramuscular injections of 10 c.c. of 10 per cent calcium gluconate were given and there was no further evidence of tetany, although the blood-calcium remained low.

The serum alkaline phosphatase had fallen from the pre-operative value of 110 K.A. units to 88 K.A. units a fortnight after operation. At six weeks following operation it had fallen to 34 K.A. units.

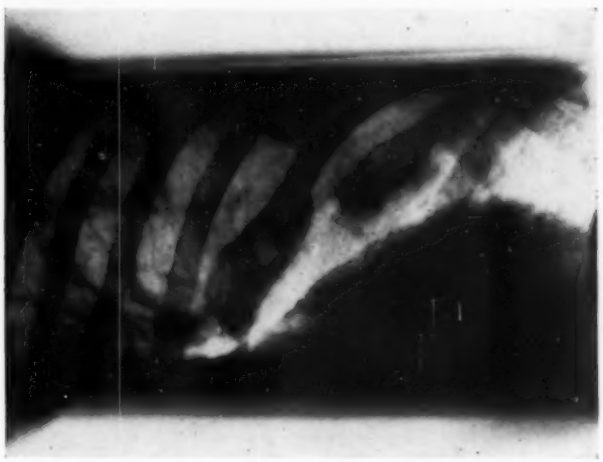

FIG. 171.—*Case* 2. Radiograph of the chest. Several fibrocystic lesions of the ribs are demonstrated. There is no generalized osteoporosis.

In the light of Albright's experience of cases with a high pre-operative alkaline serum-phosphatase it was not anticipated that the blood-calcium would return to a normal value for a period of two months or so. In this period, the bones, 'greedy for calcium', avidly absorb all available calcium, the amount in the circulation remaining low until satisfactory recalcification has occurred. The post-operative metabolism in this case can be contrasted with *Case* 3, where a relatively lower pre-operative serum alkaline phosphatase level presaged a less dramatic fall in blood-calcium and absence of tetany.

When seen in the Outpatients' Department six weeks following operation, bone pain had returned. A blood-calcium estimation was 7·6 mg./100 ml. Daily intramuscular injections of 10 c.c. 10 per cent calcium gluconate were prescribed for the ensuing three weeks with considerable benefit. Ten weeks following operation, bone pain had ceased and the blood-calcium had risen to 8·7/100 ml.

Case 3.—This patient had been previously treated on separate occasions for a solitary bone cyst and an epulis of the lower jaw. The diagnosis was established at a later date when, following a shoulder injury, a radiograph demonstrated a cystic lesion in the head of the right humerus and a fracture of the acromion. Other bone lesions were then discovered and the presence of hypercalcæmia established.

Mrs. N., aged 41, was first seen complaining of a solitary cystic swelling of the right tibia; this was treated by curettage and grafting in February, 1949. A histological report on the material removed suggested the lesion to be a benign osteoclastoma. Subsequent radiological examination of the skeleton showed some punched-out areas in the phalanges of both hands but without changes elsewhere. A serum-calcium estimation at this time was 12·6 mg. per cent and the plasma-phosphatase was within normal limits. It was considered that a diagnosis of hyperparathyroidism was unlikely.

In February, 1950, a complete radiological examination of the skeleton failed to reveal any characteristic changes, but in May, 1950, a giant-celled epulis was removed from the lower jaw.

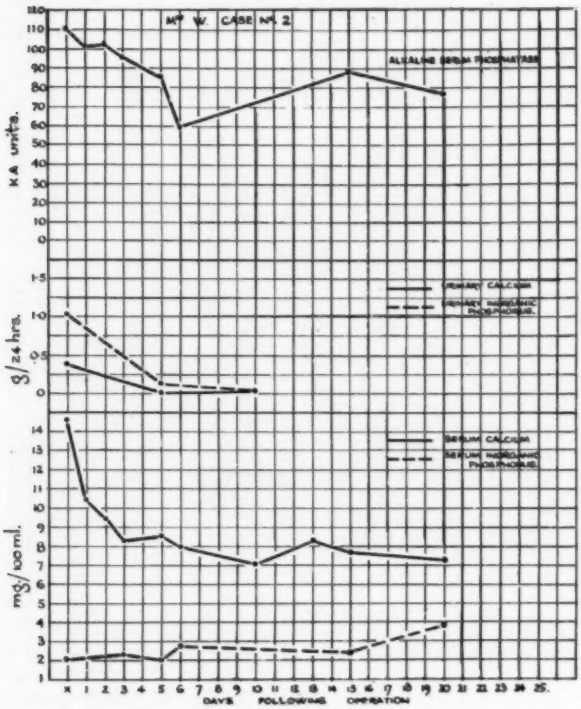

FIG. 172.—*Case* 2. Relevant pre- and post-operative biochemical investigation.

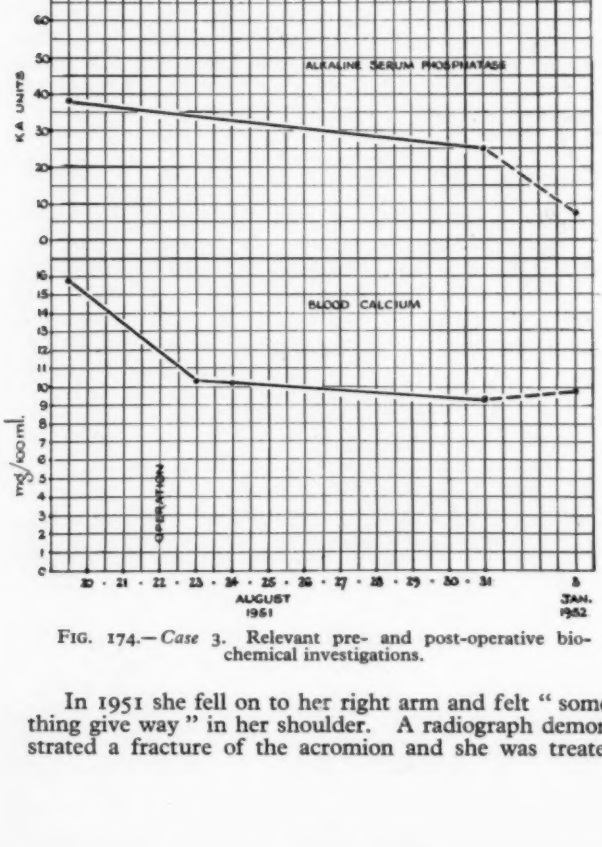

FIG. 174.—*Case* 3. Relevant pre- and post-operative biochemical investigations.

In 1951 she fell on to her right arm and felt "something give way" in her shoulder. A radiograph demonstrated a fracture of the acromion and she was treated as an out-patient. On her next visit a re-X-ray examination demonstrated an area of rarefaction in the outer rim of the clavicle and a small cyst in the shaft of the humerus. The possibility of multiple myelomatosis was

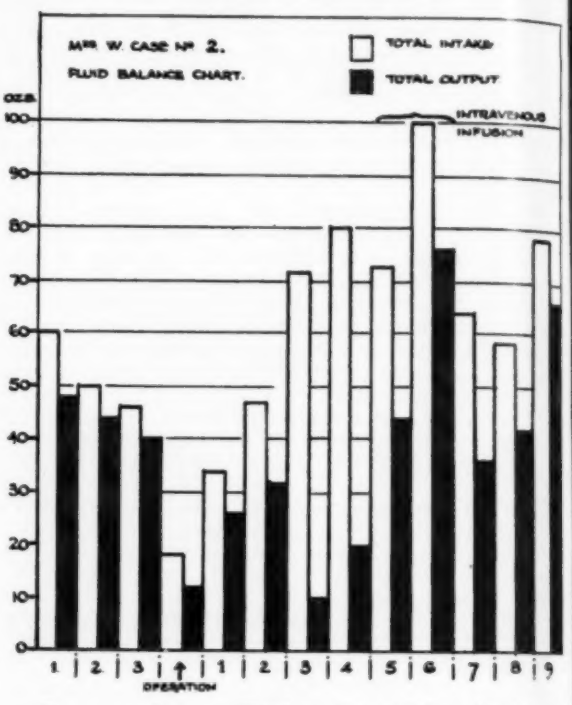

FIG. 173.—*Case* 2. Showing post-operative oliguria.

considered, but a normal serum-protein level and a normal marrow examination rendered this diagnosis unlikely. Radiological examination of the whole skeleton was then performed. The results were consistent with a diagnosis of hyperparathyroidism, viz. :—

Hands: There is subperiosteal bone absorption in some of the phalanges. It is most marked in the middle phalanges of the outer fingers.

Pelvis: The right superior pubic ramus is porotic and its normal architecture destroyed. Trabeculæ cross the porotic area, causing a multilocular cystic appearance.

Skull; There is a finely stippled bone pattern of the vault.

Right Clavicle: There is an expanding lesion at the outer end of the right clavicle.

Right Humerus: There are three defined areas of porosis in the shaft of the right humerus, situated in the medulla and thinning the bone cortex by erosion of its inner aspect.

Ribs: There is a small cyst, without expansion, of the 11th rib. There is a fracture through a similar lesion of the 8th rib.

Renal Tract: There are some small areas of calcification in the upper parts of the right and left kidney, which suggest nephrocalcinosis.

Full biochemical investigation was performed with the following findings :—

Serum-calcium (July 27, 1951), 15 mg. per cent.

Serum-inorganic phosphorus, 3·3 mg. per cent.

Serum alkaline phosphatase, 31 K.A. units.

Serum-protein, 7 g. per cent. Globulin, 2·5 g. per cent; albumin, 4·5 g. per cent.

Blood-urea, 36 mg. per cent.

Urea-clearance test, 44 per cent and 65 per cent of normal.

Urinary calcium (24-hour specimen vol. 2330 ml.), 0·669 (N = 0·01-0·3 g.).

Urinary inorganic phosphatase (24-hour specimen vol. 2330 ml.), 0·989.

A confident diagnosis of hyperparathyroidism was made. At operation (Professor Brockman, Aug. 22), a large adenoma was removed from the left lower position.

HISTOLOGY OF ADENOMA.—The parathyroid adenoma received consists of typical columns of cells separated by wide sinusoidal blood-vessels. The cells are almost entirely of the clear-cell type having a dark nucleus and a pale cytoplasm. No eosinophil cells are seen.

There was marked constitutional improvement following operation, and, as the results of the biochemical tests demonstrate, calcium metabolism returned to normal (*Fig.* 174). In spite of this evidence of cure, however, there was progressive increase in the size of the lesions demonstrated pre-operatively in the right ilium, right clavicle, and right humerus. This extension of the lesions was demonstrated by serial radiographs taken during the six months following operation. By June, 1952, however, re-calcification was occurring satisfactorily in all the lesions. To date she remains well and is free of symptoms.

Case 4.—W. S., a male patient aged 58, was first seen in 1946 complaining of pain in the right tibia for two to three years. On examination there was some diffuse swelling on the upper half of the right tibia, but no other abnormal physical findings. On the first occasion the right leg only was radiographed and the radiological report was suspicious of Paget's disease. He received a course of deep X-ray therapy to the right tibia and this was followed by a remission of symptoms. He was seen again in 1949 with pain in the left leg, and a painless nodule was found in the right tibia. The patient was admitted to hospital in November, 1949, and the results of biochemical investigation were :—

Serum-calcium, 16·2 mg. per cent.

Serum inorganic phosphorus, 2·4 mg. per cent.

Serum alkaline phosphatase, 82 K.A. units.

Total serum-protein, 5·1 g. per cent ; serum-albumin, 2·6 g. per cent ; serum-globulin, 2·5 g. per cent.

Bence-Jones protein : None detected in urine.

The bone-marrow examination showed no evidence of myeloma but was suggestive of hyperparathyroidism.

RADIOLOGICAL EXAMINATION was as follows : The appearances were typical of hyperparathyroidism and also of localized Paget's disease of the right tibia.

Skull : Fine pin-point stippling of the bones of the vault with some generalized osteoporosis.

Hands : There is generalized bone porosis with a cyst in the right metacarpal (*Fig.* 175). There is marked subperiosteal bone absorption of the phalanges of both hands—particularly of the radial borders—leaving a fine network of projecting delicate spicule-like trabeculæ. The tufts of the terminal phalanges showed bone absorption producing a cystic appearance and a scalloped margin (*Fig.* 176).

R. Tibia : The upper two-thirds show an abnormal bone architecture with thick irregular trabeculation. The affected bone is considerably expanded, suggestive of Paget's disease.

L. Tibia : Two oval translucencies in its middle third.

R. Scapula : The acromioclavicular joint is increased in width and there is teasing out of the bone structure of the outer end of the clavicle.

Ribs : Cystic lesions in fifth and sixth ribs.

Dorsal and Lumbar Spine : No abnormality.

Summary.—Some generalized osteoporosis with pin-point porosis of the skull. Cystic lesions of several of the long bones and marked subperiosteal resorption of the phalanges, clavicle, humerus, and radius. Paget's disease of the right tibia was present.

These findings confirmed hyperparathyroidism ; the renal function was found to be normal and this excluded secondary hyperparathyroidism due to chronic renal disease. The hyperparathyroidism was considered to be due to a parathyroid adenoma, but the patient declined an operation. He remained well until February, 1952, when he developed a prominent swelling in the right clavicle about 5 cm. in diameter and this subsequently

FIG. 175.—*Case* 4. Radiograph of the hand, demonstrating bone resorption, most marked on the radial aspect of the intermediate phalanges and in the terminal phalanges. There is a fibrocystic lesion in the head of the third metacarpal.

gave rise to a spontaneous fracture in February, 1953. This case is being followed carefully for subsequent progress of the bony lesions and later nephrocalcinosis.

Case 5.—Mrs. N., aged 30. The aching pains in the limbs and chest, frequency of micturition, and hæmaturia were the presenting features of this case. The underlying hyperparathyroidism was not diagnosed and a functional basis for these symptoms suggested. At a much later date radiology demonstrated osteodystrophy and nephrocalcinosis. Pathological fracture occurred while the patient was awaiting admission.

HISTORY.—This patient first attended the surgical out-patient department in June, 1950, complaining of hæmaturia. She stated that for two or three years she had been feeling generally unwell, had frequency of micturition, and experienced many bouts of nausea and vomiting. For a year she had noticed weakness of both arms, pain in the chest, and what she described as ' rheumatism ' in her legs.

A complete urological examination failed to determine the cause of hæmaturia. She continued to attend the out-patient department, and for a time her symptoms improved.

In August, 1951, her condition became worse, with severe pain in both legs and progressive muscular asthenia. Amenorrhœa had been present for five months.

A provisional diagnosis of hysteria was made in consultation with a psychiatrist, but the possibility of hyperparathyroidism was considered and subsequently confirmed by biochemical and radiological examination, viz. :—

1. Serum-calcium, 14·8 mg./100 ml.
2. Serum alkaline phosphatase, 78 units.
3. Radiological examination :—

Spine and Pelvis: Marked generalized osteoporosis with a coarse, sparse, trabecular pattern.

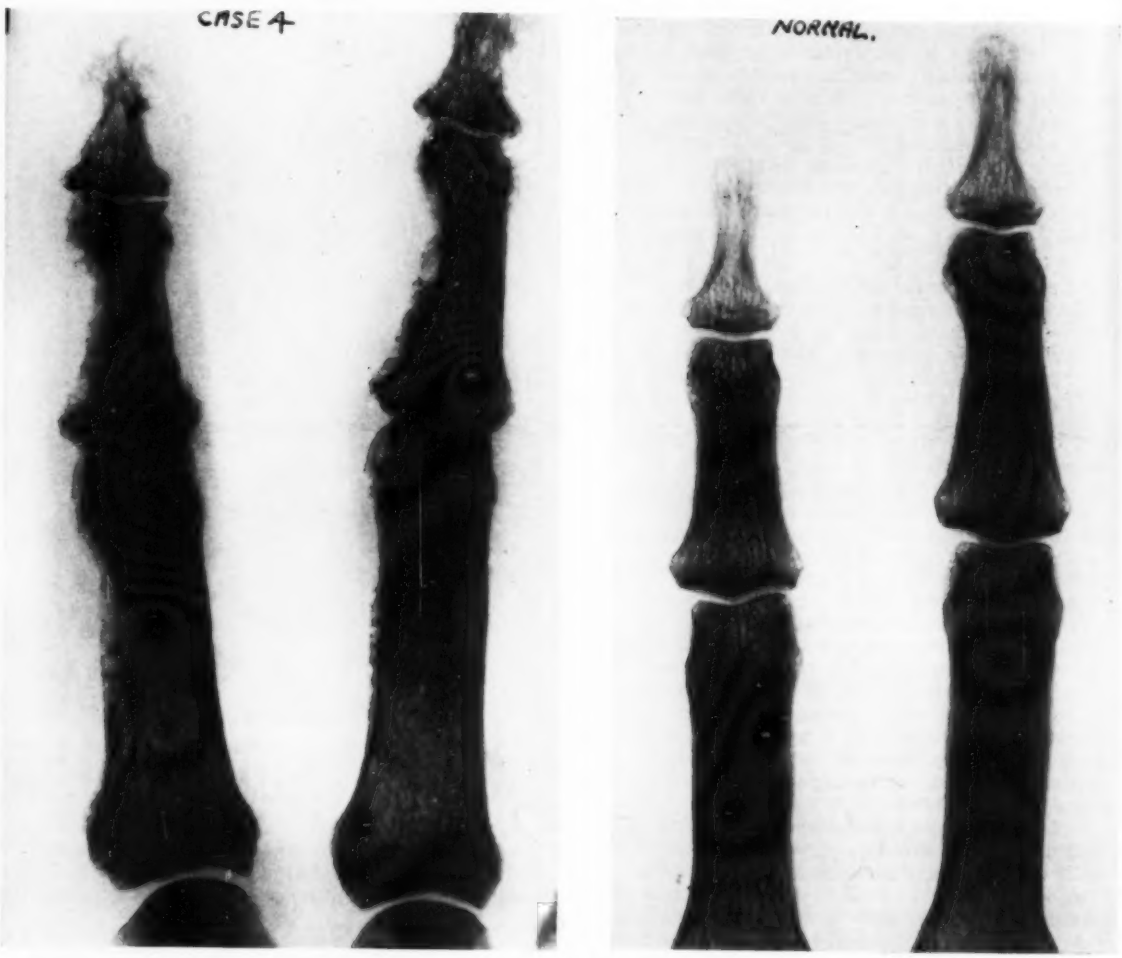

FIG. 176.—*Case* 4. Bone resorption of phalanges with a radiograph of normal phalanges for comparison.

Skull: Marked generalized osteoporosis with small rounded areas of normal bone density (*Fig.* 177). Marked osteoporosis of the facial bones and mandible.

Ribs: Localized expanding translucent lesion of the fifth rib through which there is a fracture.

Renal Tract: Extensive calcification of both kidneys, the configuration of which was consistent with calcification of the renal pyramids (*Fig.* 178). No abnormality was demonstrated on excretion urography.

She was put on the waiting list for urgent admission. On Oct. 9, 1951, she tripped and fell in her home and was admitted to hospital with pathological fracture of both femurs. Further radiological examination revealed marked porosis of the femora with fractures of the middle third of the shaft in each case. Thomas splints were applied under a general anæsthetic. Clinical examination revealed a palpable nodule in the lower part of the left anterior triangle of the neck. At operation (Mr. W. J. Lytle) on Oct. 13, 1952, a large thyroid adenoma was easily found and removed from its position behind the lower pole of the left lobe of the thyroid.

HISTOLOGICAL REPORT ON SPECIMEN.—The section shows the classical structure of a benign parathyroid adenoma which is mainly of the clear-cell type; the cells are arranged in rather compact cords and are supported by a small amount of vascular stroma. The cells are of moderate size and polyhedral, are uniform in shape and size, and are arranged in an orderly mosaic pattern. The cells have a single central, rounded vesicular nucleus with a ballooned and empty cytoplasm. There is evidence of both recent and old hæmorrhages.

SUBSEQUENT PROGRESS.—The response to the removal of the tumour was indicated by the subsequent serum-calcium estimations (*Fig.* 179), and bone pain disappeared immediately after the operation. She developed clinical evidence of tetany five days after operation. This responded to intramuscular injection of calcium gluconate 10 c.c. of a 10 per cent solution twice daily. Injections were continued for three weeks.

There was clinical and radiological evidence of union of both fractures by the beginning of January, 1953. She was allowed up in callipers at the end of the month. When seen in April, 1953, she was walking with the aid of a stick alone. Her general health has improved markedly and her menses have recommenced. Frequency of micturition has ceased. X-ray studies demonstrate re-calcification of the previous osteoporotic lesions. Calcification of the renal pyramids remain unchanged.

Case 6.—Mrs. G., aged 39. This patient's investigations were incomplete, but there is very strong presumptive evidence of hyperparathyroidism.

HISTORY.—In 1943 a pyelolithotomy was performed for a right-sided renal calculus. She complained of two years' pains in both legs, diagnosed by her own doctor as 'arthritis'. She also suffered from lassitude and was admitted to hospital in November, 1952, with right-sided abdominal pain and frequency of micturition.

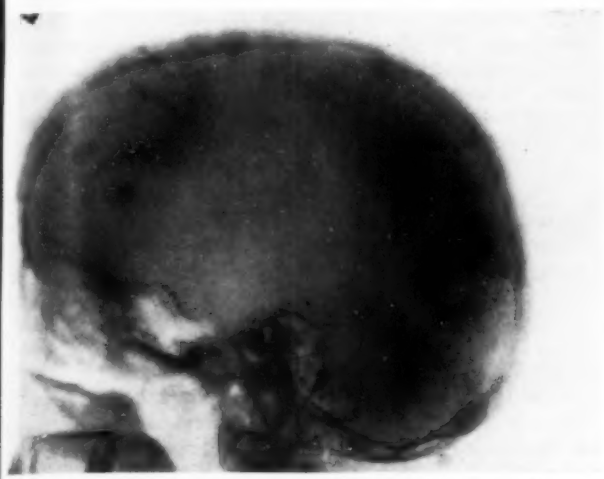

FIG. 177.—*Case* 5. Radiograph of the skull. Generalized osteoporosis is demonstrated with a coarse type of mottling simulating Paget's disease.

FIG. 178.—*Case* 5. Excretion pyelography. Nephrocalcinosis is demonstrated involving the renal pyramids.

Pyelitis was diagnosed and she was treated successfully with an alkaline mixture (mist. pot. cit. N.F.). Further investigations were as follows :—

RADIOLOGY.—

1. *Renal Tract.*—

a. Straight film: Several small discrete calcified opacities overlie the shadow of the upper pole of the right kidney. A calcified opacity overlies the lower pole of the left kidney.

b. Intravenous pyelogram: Adequate and symmetrical excretion is demonstrated. The calcified opacities are shown to lie just lateral to the cups of the minor calices and correspond in position to the renal medullary pyramids.

2. *Skull.*—The bone pattern shows a fine stippled porosis particularly marked over the vault. Whilst not definitely abnormal, the appearances are consistent with hyperparathyroidism.

3. *Chest.*—No abnormality.

4. *Pelvis.*—No abnormality.

5. *Left Femur.*—No abnormality.

BLOOD-CHEMISTRY (Jan. 26, 1953).—

Serum-calcium, 13·1 mg./100 ml.

Serum inorganic phosphorus, 4 mg./100 ml.

Alkaline serum phosphatase, 13 K.A. units.

URINE.—Sulkowitch test for calcium—positive.

Further investigations were contemplated, but the patient discharged herself from hospital and has failed to attend the follow-up clinic.

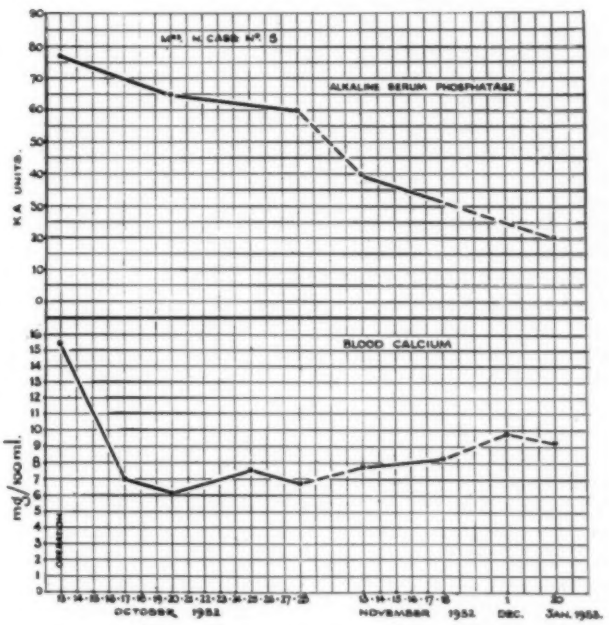

FIG. 179.—*Case* 5. Relevant pre- and post-operative biochemical investigations.

PHYSIOLOGICAL CONSIDERATIONS

In health the total serum-calcium is between 9 and 11 mg. per cent. This consists of: (*a*) Non-diffusable calcium bound to protein, usually 4–5 mg. per cent, and fluctuating according to the level of the serum-proteins (McLean and Hastings, 1935); (*b*) Calcium ions which are freely diffusable and usually total 4·75–6·25 mg. per cent; (*c*) A small unionized but diffusable quantity (0·25 mg.) of calcium in the form of organic salts such as calcium citrate. The solubility product of calcium and phosphate ions in the serum is a constant and this means that a rise in calcium ions leads to a fall in phosphate ions and vice versa. Normally the serum is physically supersaturated with both these ions.

This mechanism is controlled by parathormone, an active hormone first isolated by Collip in 1925.

An overproduction of parathormone such as that produced by a parathyroid adenoma will produce the following abnormal physiological and biochemical changes :—

Elevation of serum-calcium.
Increase in urinary calcium excretion.
Increased urinary phosphate excretion.
Decreased serum inorganic phosphates.
An increase in the alkaline serum phosphatase.

There is still no unanimity of opinion regarding the method by which hyperparathyroidism produces such biochemical and biophysical changes. The main hypotheses are those of Thomson and Collip (1932), Jaffe (1933), and Albright and Reifenstein (1948); the theory of the last authors has been most widely accepted.

Thomson and Collip believed that parathormone stimulates osteoclastic activity, leading to widespread lacunar absorption. The liberated calcium and phosphate is absorbed into the circulation, the excess being excreted by the kidneys. Calcium is not removed from bone by a process of demineralization, decalcification, or 'halisteresis', but is always removed from bone with its associated organic matrix by a process of local osteoclastic bone absorption. Milne (1951), after experimental observations on human calcium metabolism, supports Thomson and Collip's theory with the statement that "the clinical effects of hyperparathyroidism would appear to be caused chiefly by the direct action of the hormone on the processes of bone resorption". A renal action of parathormone was shown to be important in hypoparathyroid states, but not in normal or hyperparathyroid individuals.

Albright asserted that the excess of parathormone acts in some way on the serum-phosphates, affecting their renal threshold so that an excess is excreted in the urine. The fall in the serum-phosphate ions results in mobilization of calcium from the bones in order to maintain the solubility product at a constant level. The serum-calcium becomes raised and any excess is excreted in the urine. The serum-alkaline phosphatase is raised as a result of excessive osteoblastic activity increased in order to replace the absorbed bone by new organic matrix. Albright's theory that parathormone "affects phosphate dissolved in body fluids in such a way as to make it more readily excreted by the kidney" is no longer tenable—at least, regarding hyperparathyroidism (Milne, 1951). Dent (1953) believes that a renal action of parathormone exists in addition to the direct action on bone. This latter author explains the low phosphate level of primary hyperparathyroidism on the basis of increased phosphate clearance by the kidney.

PATHOLOGY

Primary hyperparathyroidism is most commonly associated with a single adenoma. Rarely more than one adenoma is present. Hyperparathyroidism associated with primary hyperplasia of all parathyroid tissue is extremely rare but has been reported by Albright, Sulkowitch, and Bloomberg (1938). Occasionally a carcinoma of the parathyroid has been associated with hyperparathyroidism.

Norris (1947), in an analysis of a large series, found that a single adenoma occurred four times as frequently in the upper than in the lower glands. He found 10 per cent of the tumours were aberrant in position, viz., mediastinal, within the thyroid gland itself, or behind the œsophagus.

The adenomata are usually well circumscribed, brownish-red in colour, soft in consistency, and often with areas of cystic degeneration. There is no constant histological pattern. They may be composed of: (1) Small or large 'chief' cells, which are larger than the corresponding cells of the normal parathyroid; (2) Large water-clear cells—the structure of such an adenoma often bears a close resemblance to that of hypernephromata; (3) Oxyphil cells. Classification into one of these distinct types is not always possible as it is common to find a mixture of all cell types. The pure oxyphil adenoma is rare. It is usually inactive and unassociated with clinical hyperparathyroidism (Keynes, 1936; Hadfield and Rogers, 1932). *Case* 1 was unusual in this respect, a purely oxyphil adenoma being associated with advanced hyperparathyroidism. Similar cases have been recorded by Hanks (1942), Ballin (1935), and Woolner (1952). The adenoma in *Case* 2 consisted of clear cells and eosinophil cells; in *Cases* 3 and 5 it consisted of clear cells only.

Hypertrophy of all four glands is usually characterized by a proliferation of water-clear cells only. These cells are larger than normal, with peripherally placed nuclei. Usually no oxyphil or chief cells can be found. Mitoses, hyperchromatism irregularity, and irregularity of nuclei in an adenoma may lead to a histological diagnosis of carcinoma. True parathyroid carcinoma associated with hyperparathyroidism is rare, though indisputable evidence of the occasional association has been noted in cases recorded by Meyer, Rosi, and Ragins (1939). Meyer and others (1939), Gentile, Skinner, and Ashburn (1941), Black (1948), de Wesselow and de Wardener (1949), and Woolner (1952).

CLINICAL FEATURES

Parathyroid adenomas occur more frequently in women. Norris (1947) reviewed 317 cases collected from the literature with a sex ratio of 3 women to 1 man. The age distribution is wide and of little importance in diagnosis, cases having been recorded as young as 16 years and as old as 74 years (Murphy, Hurxthal, and Dell, 1952). The clinical features are often protean and fall into four main categories.

1. Bone.—Symptoms may be due to the progressive osteoporosis. The initial symptoms are vague and consist of aching pains often misinterpreted as of rheumatic or arthritic origin. Eventually bony deformity may occur and the kyphoscoliosis, pigeon chest, and pelvic deformity of the fully developed case is well exemplified in *Case* 1. This osteodystrophy presents a similarity to osteomalacia, rickets, and polyostotic fibrous dysplasia. Bony swellings may occur and are especially noted in the clavicle, ribs, mandible, and long bones. Such swellings may be bone cysts or solid tumours histologically similar to benign osteoclastomata. For example, in *Case* 3 an osteoclastoma was curetted two years before the diagnosis of hyperparathyroidism was established. Pathological fracture through osteoporotic bone or through a cystic area occurs in severe cases (*Cases* 3 and 5).

Another occasional finding in hyperparathyroidism is a myeloid epulis. Such a lesion preceded the ultimate diagnosis in *Case* 3 by twelve months. Hyperparathyroidism had been suspected in this case in the previous year at the time of treatment of a tibial osteoclastoma, but normal blood chemistry was misleading. A similar case was recorded by Levy (1952). Osteodystrophy of the mandible

(Cahn, 1948) may be the earliest sign of hyperparathyroidism, and this is attributed to the repeated minor trauma of mastication. Albright (1933) reports the absence of the lamina dura as an early feature of hyperparathyroidism, and occasionally the discovery of the disease was made by the dental department.

2. Renal.—Polyuria and polydipsia is often a marked clinical feature of hyperparathyroidism. Albright and Reifenstein (1948) suggest that this may be due to the increased excretion of calcium and phosphate. Prolonged hypercalcæmia may cause calcium deposition in the tubules leading to a polyuria from malabsorption of fluid and electrolytes. The oliguria which follows the removal of a parathyroid tumour suggests that the polyuria is related to the hypercalcæmia *per se*, and is not necessarily due to tubular calcification.

Chute (1939) found that 84 per cent of his patients with parathyroid adenomas and hyperparathyroidism had urinary calculi. Norris (1947) found that 118 out of 322 cases of parathyroid tumours showed evidence of calculi. Nephrocalcinosis or nephrolithiasis may precede the onset of bony changes by many years. It is important that patients with bilateral renal calcification should be investigated—to exclude hyperparathyroidism. In *Case* 5, which presented with bilateral renal calcification, there is strong presumptive evidence of hyperparathyroidism without gross bony changes.

3. General.—General symptoms such as lassitude, muscle weakness, nausea or vomiting, and constipation frequently occur and have been attributed to the hypercalcæmia (Morelle, 1932). Barr and others (1930) described a case with extreme hypotonicity of the muscles, and Hunter and Turnbull (1931) noted a diminution in auditory acuity restored by removal of the parathyroid adenoma. Fitz and Hallman (1952) report the occasional occurrence of psychoses associated with hyperparathyroidism. Ballin and others (1935) noted calcification in the ear drums in a patient with hyperparathyroidism. Severe attacks of vomiting, constipation, lassitude, and muscle weakness were noted in several cases in the present series. Electrocardiographic changes occur owing to the hypercalcæmia of hyperparathyroidism and Graybiel and White (1941) noted a shortening of the Q-T interval owing to a diminution in the length of ventricular systole. Hypercalcæmia manifests itself in another fashion by causing calcification in the superficial layers of the periphery of the cornea leading to a lesion described by Cogan (1947) as a ' band keratitis '. Walsh and Howard (1947) found deposits in the deep conjunctiva of the palpebral fissure on visualization with a slit lamp, and Fleischner and Shalek (1949) also emphasized the occasional occurrence of similar ocular lesions. No cases in the present series showed ocular calcification.

4. Hyperparathyroid Crisis.—In rare cases hyperparathyroidism may be severe and give rise to intense hypercalcæmia and ' parathyroid poisoning '. This is a biochemical death due to the gross metastatic deposit of calcium in almost every organ. Dawson and Struthers (1923) described the autopsy details of a case with calcium deposits in all the internal organs, notably arteries, heart, stomach, and lungs.

Smith and Cooke (1940) reviewed 4 cases of hyperparathyroid crisis and described a case of their own with calcification and necrosis in the kidneys and pancreas. Rogers (1946) reported 2 patients with duodenal ulcer and hyperparathyroid crisis; both patients died. This association of duodenal ulcer with fatal hyperparathyroid crisis has been reviewed by many other authors (Rogers, Keating, Morlock, and Barker, 1947; Robinson, Black, Sprague, and Tillisch, 1951; Elkeles, 1953). The high calcium and alkali content of a gastric diet may be dangerous in a patient with already established hyperparathyroidism.

DIFFERENTIAL DIAGNOSIS

Hyperparathyroidism due to parathyroid adenoma must be differentiated from: (1) Hyperparathyroidism secondary to chronic nephritis; (2) Hyperparathyroidism due to bony metastases; (3) Primary bone diseases, such as, for example, Paget's disease or multiple myeloma; (4) Other diseases, e.g., diabetes insipidus or mellitus.

' Renal Rickets ' or ' Renal Osteodystrophy '.—In patients with chronic renal insufficiency, a constant acidosis leads to an increased excretion of calcium in the urine as base. Phosphate is retained owing to glomerular impairment, and a high serum-phosphate with a low serum-calcium results. The skeletal deformities result from constant de-ossification and new osteoid formation in a similar fashion to primary hyperparathyroidism, but the biochemical picture of acidosis, NPN retention, low serum-calcium, and high serum-phosphate is sufficiently diagnostic.

Occasionally, tubular insufficiency may occur in chronic nephritis without glomerular insufficiency, and in this type of renal rickets the compensatory parathyroid stimulation leads to a phosphorus diuresis and eventually both a low serum-phosphate and low serum-calcium. Careful biochemical analysis is necessary to distinguish renal rickets from nephrocalcinosis due to a parathyroid adenoma, and the finding of a raised serum-calcium always favours the latter. Albright (1948) points out that in primary hyperparathyroidism the serum-calcium may not be markedly raised even in the presence of a doubled urinary calcium excretion, and a 24-hour calcium excretion is important in differential diagnosis. The radiological differentiation will be discussed later.

Secondary Parathyroid Hyperplasia due to Bony Metastases.—Swyer (1950) describes the occurrence of secondary hyperparathyroidism in patients suffering from osteoclastic secondaries from carcinoma of the breast. This author suggests that the metastases in some unknown fashion produce a secondary stimulation of the parathyroid gland. Although the syndrome described by Berger is uncommon, some diagnostic difficulty was experienced in *Case* 1 of the present series where a coincident carcinoma of the stomach suggested the possibility of bony secondaries. A bone-marrow examination or bone biopsy might prove helpful in the differential diagnosis of osteoclastic secondaries and secondary hyperparathyroidism.

Primary Bone Diseases.—Hyperparathyroidism with bony changes must be differentiated from primary bone diseases, e.g., multiple myeloma,

osteoporosis, osteomalacia, Paget's disease, polyostotic fibrous dysplasia, and other diseases such as Gaucher's disease and xanthomatosis. The biochemical picture of increased serum-calcium, increased urinary calcium, decreased serum-phosphate and raised alkaline phosphatase is usually diagnostic.

Other Diseases.—The polyuria, polydipsia, vomiting, and weakness may occasionally give rise to the clinical suspicion of diabetes mellitus or diabetes insipidus. The biochemical features of hyperparathyroidism rapidly clarify this difficulty.

RADIOLOGICAL FEATURES OF HYPERPARATHYROIDISM

There are five radiological manifestations of parathyroid over-activity, of which three are abnormalities of the bony skeleton.

1. Generalized Osteoporosis.—This is manifested radiologically by a diminution of the radiodensity of the bone of the entire skeleton. The trabecular architecture of the bone becomes altered; fewer, finer, and more irregular trabeculæ are seen, producing a pattern coarser than normal. The bone cortex tends to retain its density but becomes thinner and may contrast with the greatly increased radiolucency of the bony medulla producing a 'pencilled outline'. This marked loss of bone structure causes the skeleton to be much weakened and inadequate to perform its supportive function. This results in such deformities as scoliosis, kyphosis, biconcave fish-shaped vertebræ, coxa vara, protrusio acetabulare, etc., as is so well demonstrated in *Case* 1. In the calvarium a more distinctive pattern of osteoporosis occurs, producing a fine pin-point or granular mottled porosis with some loss of distinction of the inner and outer tables. It is believed that this appearance of the vault of the skull is very common and very suggestive of hyperparathyroidism, although in some cases there is a coarser mottling of the skull indistinguishable from Paget's disease (*Cases* 1 and 5). Fractures, particularly of the ribs, long bones, and through fibrocystic lesions, and either complete or incomplete (Looser's zones), occur with little or no preceding trauma; they unite with adequate callus formation.

2. Localized Fibrocystic Lesions of Bone.—Excessive local destruction of bone produces a fibrocystic lesion indistinguishable radiologically from an osteoclastoma. The bone is commonly expanded, sometimes markedly so; the cortex is thinned, and the cyst-like translucency is usually traversed by sparse trabeculæ. These fibrocystic lesions may occur in any bone, particularly the ribs, jaws, and pelvis; they are usually multiple, often occurring at different stages in the evolution of the disease (*Case* 2), and they may be unaccompanied by obvious generalized bone porosis (e.g., *Cases* 2 and 3).

3. Subperiosteal Bone Resorption.—This phenomenon was first accurately described by Camp and Ochsner in 1931, and is the most valuable and diagnostic single radiological sign of hyperparathyroidism. In recent years it has again been occasionally reported, but usually as a lacework periosteal new-bone formation. This is erroneous as new bone is not being deposited but the old bone is being removed by excessive osteoclastic activity in the subperiosteal zone. This sign has been neglected, and often omitted, in most of classical radiological and clinical text-books.

Recently Pugh (1952) has investigated this particular type of bone absorption and has found that it occurs only in the presence of excessive parathyroid activity—either a primary over-activity or a parathyroid hyperplasia secondary to other conditions, e.g., chronic renal failure. This radiological sign is thought to be pathognomonic of hyperparathyroidism, and if chronic renal disease can be excluded it is indicative of primary hyperparathyroidism.

Subperiosteal bone absorption is seen most frequently and most convincingly in the phalanges of the hands. Usually the middle phalanges are most affected, particularly their radial border, which becomes markedly concave owing to cortical and subcortical bone absorption. The cortex is lost and the outline of the eroded or lattice pattern with fine, thin, short trabeculæ projecting from the bone medulla into the zone previously occupied by the cortex. It is usual to find associated with this change an abnormal bone texture of the phalanges. The distinction between the cortex and the medulla is lost, and the bone pattern takes the form of a rather coarse meshwork or reticulation with blurring of bone detail.

The terminal phalanges are similarly affected and the terminal tuft becomes absorbed, often producing a scalloped outline. Occasionally the whole of the tuft and the shaft of the terminal phalanges are absorbed, and this is usually accompanied by clinical evidence of shortening of the fingers and clubbing.

Periosteal bone resorption also occurs, but less commonly, and more difficult of detection, in other bones. It has been noticed at the lower end of the radius and ulna, below the inner condyle of the tibia, the greater trochanter of the femur, and the acromioclavicular joint. At this latter site there is widening of the joint space with loss of cortical bone, and fraying or teasing out of the denuded articular surfaces, which may be cupped (Nathanson and Slobodkin, 1950).

Loss of the dental lamina is commonly found in hyperparathyroidism, and is another manifestation of subperiosteal bone resorption, the lamina dura representing cortical bone. Loss of the lamina occurs in other generalized diseases of bone, e.g., osteomalacia and Paget's disease, and as the lamina dura is not present in edentulous patients its absence is not as reliable or as valuable a sign of hyperparathyroidism as phalangeal subperiosteal bone absorption.

4. Renal Changes.—Calcium phosphate calculi are deposited in the calices; they are commonly small and multiple, occurring in several calices of both kidneys. The calculi may become much larger and eventually form a staghorn cast of the renal pelvis and calices.

Urinary calcium may also be deposited in the renal tubules and in the connective tissue of the kidney, to which condition the term 'nephrocalcinosis' is applied. This deposition may be orderly and linear along the medullary rays, forming a series of fine lines of calcification arranged fan-wise at the site of each renal pyramid. Alternatively the calcification may be mottled and stippled, outlining the renal pyramids (e.g., *Case* 5).

5. Visceral Calcification.—Arterial calcification is often found in hyperparathyroidism, and many of the named peripheral arteries and their smaller branches may be demonstrable radiologically. Calcification may also be demonstrated in the lungs, visceral lymph-glands, myocardium, and stomach.

6. Parathyroid Glands.—If the hyperparathyroidism be due to a parathyroid tumour, the latter may be occasionally demonstrated by soft-tissue radiography of the neck or may be found deforming the œsophagus in the neck or mediastinum. Occasional cases of calcification in the tumour have been reported and diagnosed on radiological examination (Elkeles, 1953).

DISCUSSION

The fully developed radiological picture of hyperparathyroidism as outlined above, is typical and pathognomonic. The diagnosis is not, however, dependent on the demonstration of all these classical features.

Marked generalized bone porosis is commonly believed to be one of the most frequent, and, possibly, an essential radiological sign of the disease. Bone porosis in its less severe degrees may be very difficult to assess even with a normal bone control, and may be variously interpreted by different, or even the same, radiologist at different times.

The absence of definite and generalized bone porosis must in no way invalidate the diagnosis of hyperparathyroidism. The reluctance to make this diagnosis or even to consider it in the presence of multiple fibrocystic lesions of bone without generalized porosis, is believed to be prevalent, and has led to much delay in making the final diagnosis in many cases (*Cases* 2, 3, and 4). Only 3 of our 6 patients had generalized bone porosis, 2 being marked; the other 3 cases, 2 of which (*Cases* 2 and 3) had fibrocystic bone lesions, had no detectable generalized loss of radio-density of the bones.

Osteoporosis of the calvarium is also very difficult to assess in view of the wide range of normal skull radiographs. We consider, however, that every one of our cases did demonstrate fine mottling and porosis of the calvarium, although the changes in *Case* 6 were doubtful. *Case* 5 and *Case* 1 had a more coarsely mottled porosis of the skull simulating Paget's disease.

The specificity of the subperiosteal bone absorption as demonstrated in the phalanges has been much underestimated in the past; all three patients (*Cases* 2, 3, and 4) who had bone changes and had their hands radiographed, demonstrated this change.

Other local bone manifestations, fibrocystic bone lesions, occurred in 4 of the 6 patients and were indistinguishable from osteoclastomata. It is thought the Paget changes in the leg of *Case* 4 was a coincidental finding.

It is estimated that bone changes occur in only a third of patients with primary hyperparathyroidism and in these cases the serum alkaline phosphatase is invariably raised. A normal value is very rarely found in the presence of osseous manifestations and much needless radiology can be therefore prevented. A radiograph of the hands and skull in every suspected case of hyperparathyroidism should provide diagnostic information, and normal findings in the presence of a raised serum alkaline phosphatase will strongly oppose the diagnosis of hyperparathyroidism.

The radiological distinction between primary hyperparathyroidism and renal osteodystrophy is not absolute, but the more frequent presence of fibrocystic osseous lesions and the less frequent arterial calcification found in the primary condition are helpful. Marked periosteal bone absorption is found in both conditions, and, as hyperparathyroidism is responsible for the bone changes in both diseases, the fundamental osseous changes are identical.

The Operation.—Only rarely is it possible to localize the site of a parathyroid adenoma before operation. In *Case* 5 the adenoma was palpable, but this is unusual. Keating and Cook (1945) found only 3 palpable adenomata in the series of 23 cases they describe. The surgeon will therefore usually operate in ignorance of the site. During the exploration both lobes of the thyroid gland should be freely exposed from one pole to the other.

If no adenoma is found in the usual anatomical positions search must be directed to the other sites where parathyroid tissue may occur. Walton (1931) described the occasional occurrence of an adenoma posterior to the thyroid fascia, detectable only after this fascia has been incised vertically. Gordon-Taylor and Handley (1937) collected 9 cases from the literature, to which they added 1 of their own in which an adenoma was found in the anterior mediastinum, and point out the occasional necessity of splitting the sternum for its removal. If search in the neck remains fruitless, Black (1952) recommends splitting the sternum at a later operation. He also advises that hyperparathyroidism be reproved before re-exploration, as devascularization of a small adenoma may have occurred during the cervical dissection. Should both explorations be negative, and hyperparathyroidism continue, Snapper (1949) advises subtotal thyroidectomy, as the adenoma may be hidden in the substance of the gland itself.

The Post-operative Course.—One of the most remarkable results of the removal of the adenoma is the immediate relief of bone pain following operation. This was noted in *Cases* 2 and 3, where severe arthritic-like pain had been present for a long period before operation. Following the removal of the tumour there is an immediate fall in the urinary calcium and phosphorus excretion. The serum-calcium falls to normal or sometimes subnormal limits within one to four days, while there is an associated rise in the plasma-phosphorus. In some cases the fall of the plasma-calcium to subnormal limits progresses to the point of tetany, and this almost always occurs when the hyperparathyroidism is complicated by advanced bone lesions, which is demonstrated in *Cases* 2 and 5. The explanation for the post-operative hypocalcæmia and tetany in these cases is to be found in the bones themselves. Following operation the decalcified bones absorb calcium from the plasma to such a degree that hypocalcæmia occurs. The remaining parathyroid tissue is insufficient to prevent this reversal. The onset of tetany can therefore in many cases be predicted, and is especially to be expected when the pre-operative serum alkaline phosphatase is of high value, indicating osteoblastic hyperactivity (Snapper, 1949). It can be seen from what has been stated

above that the correct treatment is the administration of calcium, usually in the form of the gluconate, and given either intramuscularly or intravenously in the form of a continuous infusion. The administration of parathormone, effective and logical in use in the treatment of tetany accompanying the accidental parathyroid removal in the course of thyroidectomy is ineffective in this condition (Albright, 1948). The serum-calcium may only return to normal when the demands of the bones have been fully met with, such a process often taking a few weeks, during which time the administration of calcium by intramuscular or intravenous injections may be necessary.

The second important immediate effect of the removal of the tumour is a temporary oliguria. This was illustrated in *Case* 2 (*Fig.* 173). Snapper (1949), discussing the cause of this oliguria, gives two adequately tenable explanations. The polyuria of hyperparathyroidism may be, in part, due to the necessity of excreting large quantities of water in order to eliminate the excessive calcium and phosphorus. Following operation this stimulus is suddenly withdrawn and overcompensation may occur resulting in oliguria. There is also evidence that parathormone may have a direct influence on renal function (Dent, 1953). The oliguria, if severe and uncorrected, may result in renal failure. An intravenous infusion should be commenced with the onset of any marked fall in urinary excretion. If, as occurred in *Case* 3, the onset of oliguria and tetany coincided, calcium gluconate may be added to the infusion, thus satisfactorily controlling both complications.

SUMMARY

1. Six cases of primary hyperparathyroidism are described. A parathyroid adenoma was successfully removed in 3 cases; 2 patients declined operation and 1 patient died from renal failure. The operation and post-operative course are discussed and the problem of aberrant parathyroid adenomas is reviewed.

2. In a case with severe bony deformity an interesting coincidental finding was a gastric carcinoma which gave rise to the clinical suspicion of bony metastases. Two patients presented with a localized bony lesion, viz.: in one case a myeloid epulis and in another case an osteoclastoma. The significance of these isolated lesions was not realized until a full osteodystrophy developed. A plea is made for full biochemical investigation in this type of case to exclude early hyperparathyroidism.

3. Renal lesions were present in 4 patients; 2 cases showed evidence of nephrolithiasis and 2 cases were found to have nephrocalcinosis. Albright and Reifenstein (1948) stress the early occurrence of renal lesions which often precede an osteodystrophy by many years, and the present cases conform to these authors' findings.

4. The differential diagnosis of primary hyperparathyroidism from renal osteodystrophy, bony metastases, secondary hyperparathyroidism due to bony metastases, multiple myeloma, Paget's disease, and diabetes, is discussed.

5. Modern views regarding the physiology of parathormone are briefly reviewed. The surgical anatomy of the parathyroids and the pathology of primary hyperparathyroidism are described. The protean clinical features of this disorder are stressed and the literature reviewed.

6. The radiological features of hyperparathyroidism are discussed with special reference to the sign of subperiosteal bone resorption first described by Camp and Oschner in 1931 and now largely neglected in most radiological text-books. This valuable diagnostic sign was seen in all 3 instances where radiographs of the hands were available. In the other 3 cases these radiographs had not been done.

We wish to thank those Consultants of the Sheffield Royal Infirmary who have allowed us to publish these cases. We also wish to express our appreciation to Sir Ernest Finch for his helpful criticism in the preparation of this paper. Mr. A. S. Foster, the medical artist, executed the diagrams with his customary skill. Mr. Coombes, of the Radiology Department, kindly prepared the X-ray reproductions.

REFERENCES

ALBRIGHT, F. (1933), *J. clin. Invest.*, **12**, 974.
— — and REIFENSTEIN, E. C. (1948), *The Parathyroid Glands and Metabolic Bone Disease*. London: Baillière, Tindall & Cox.
— — SULKOWITCH, H. W., and BLOOMBERG, E. (1938), *Arch. intern. Med.*, **62**, 199.
ASKANAZY, F. (1902-4), *Tübing. path. Anat. Inst. Anat.*, **4**, 398.
BARNEY, J. D., and GERSHWIN, B. S. (1936), *Brit. J. Urol.*, **18**, 56.
— — and MINTZ, E. R. (1937), *Arch. Surg., Chicago*, **37**, 746.
— — SULKOWITZ, H. W. (1937), *J. Urol.*, **37**, 746.
BARR, D. P., and BULGER, H. A. (1930), *Amer. J. med. Sci.*, **179**, 449.
BELLIN, D. E., and GERSHWIN, B. S. (1935), *Amer. J. med. Sci.*, **190**, 519.
BLACK, B. M. (1948), *Proc. Mayo Clin.*, **23**, 8.
— — (1952), *Surg. Clin. N. Amer.*, **32**, 1031.
CAHN, L. (1948), *Oral Surg.*, **1**, 917.
CAMP, J. D., and OSCHER, H. C. (1931), *Radiology*, **7**, 63.
CHUTE, R. (1939), *J. Urol.*, **41**, 762.
COGAN, D. E. (1947), unpublished data quoted by ALBRIGHT and REIFENSTEIN (1948).
COLLIP, J. B. (1925), *J. biol. Chem.*, **63**, 395.
DAWSON, J. W., and STRUTHERS, J. W. (1923), *Edinb. med. J.*, **30**, 421.
DENT, C. E. (1953), *Proc. R. Soc. Med.*, **46**, 291.
DE WESSELOW, O. L. V., and DE WARDENER, H. E. (1949), *Lancet*, **1**, 820.
ELKELES, A. (1953), *Lancet*, **1**, 771.
FITZ, T. E., and HALLMAN, B. L. (1952), *Arch. intern. Med.*, **89**, 547.
FLEISCHNER, F. B., and SHALEK, S. R. (1949), *New Engl. J. Med.*, **241**, 863.
GENTILE, R. J., SKINNER, H. L., and ASHBURN, L. L. (1941), *Surgery*, **10**, 793.
GORDON-TAYLOR, G., and HANDLEY, R. S. (1937), *Brit. J. Surg.*, **25**, 6.
GRAYBRIEL, A., and WHITE, P. D. (1941), *Electrocardiography in Practice*, 106. Philadelphia: W. B. Saunders.
HADFIELD, G., and ROGERS, M. (1932), *J. Path. Bact.*, **35**, 259.
HANK, H. (1932), *Arch. klin. Chir.*, **172**, 366.
HUNTER, D., and TURNBULL, H. M. (1931), *Brit. J. Surg.*, **19**, 203.
JAFFE, H. L. (1933), *Arch. Path. (Lab. Med.)*, **16**, 63, 236.
KEATING, F. R., and COOK, E. N. (1945), *J. Amer. med. Ass.*, **129**, 994.

KEYNES, G. (1936), *Brit. J. Surg.*, **24**, 403.
KLEMPERER, P. (1923), *Surg. Gynec. Obstet.*, **36**, 11.
LEVY, B. (1952), *Oral. Surg.*, **5**, 549.
MCCLEAN, F. C., and HASTINGS, A. B. (1935), *Amer. J. med. Sci.*, **189**, 601.
MANDL, F. (1926), *Zbl. Chir.*, **53**, 260.
MEYER, K. A., and RAGINS, A. B. (1943), *Surgery*, **14**, 282.
— — ROSI, P. A., and RAGINS, A. B. (1939), *Ibid.*, **6**, 190.
MILNE, M. (1951), *Clin. Sci.*, **10**, 471.
MORELE, J. (1932), *J. Chir., Brux.*, **31**, 381.
MURPHY, R., HURXTHAL, L. M., and BELL, G. O. (1952), *Arch. intern. Med.*, **89**, 783.
NATHANSON, L., and SLOBODKIN, M. (1950), *Radiology*, **55**, 30.
NORRIS, E. H. (1947), *Int. Abstr. Surg.*, **84**, 1.
PUGH, D. G. (1952), *Surg. Clin. N. Amer.*, **32**, 1071.
ROBINSON, A. W., BLACK, B. M., SPRAGUE, R. G., and TILLISCH, T. H. (1951), *Proc. Mayo Clin.*, **26**, 441.
ROGERS, H. M. (1946), *J. Amer. med. Soc.*, **130**, 22.
— — KEATING, F. R., jun., MORLOCK, C. G., and BARKER, N. W. (1947), *Arch. intern. Med.*, **79**, 307.
SMITH, F. B., and COOKE, R. T. (1940), *Lancet*, **2**, 650.
SNAPPER, I. (1949), *Medical Clinics on Bone Diseases*. New York: Interscience Publishers.
SWYER, A. J., BERGER, J. S., GORDON, H. M., and LASZLO, D. (1950), *Amer. J. Med.*, **6**, 689.
THOMSON, D. L., and COLLIP, J. B. (1932), *Physiol. Rev.*, **1**, 309.
WALSH, F. B., and HOWARD, J. E. (1947), *J. clin. Endocrin.*, **7**, 644.
WALTON, A. J. (1931), *Brit. J. Surg.*, **19**, 285.
WOOLNER, L. B. (1952), *Cancer*, **5**, 1069.

THE MANAGEMENT OF ACCIDENTAL INJURIES AND DELIBERATE RESECTIONS OF THE URETER DURING EXCISION OF THE RECTUM

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ONE of the most important structures that regularly presents in the operative field during excision of the rectum is the ureter, and in the performance of this operation the surgeon must be constantly on his guard against injury to this structure. By a careful dissection of the ureter at strategically vulnerable points damage can usually be avoided, but the fact remains that, even in experienced hands, injuries still occasionally occur. Particularly is this so when adherent growths, which have distorted the normal anatomy, are being removed. It is also true that in the management of advanced neoplasms of the rectum surgeons are now adopting a more aggressive attitude, and, where a ureter is firmly fixed to the growth, they do not hesitate to carry out a deliberate partial ureteric resection. Indeed, it will probably be found that the greater the surgeon's experience of this type of surgery, the smaller will be his incidence of accidental injury, but the higher the proportion of patients in whom he is prepared to undertake a planned resection of the ureter in association with an adherent growth.

In order to define some of the problems associated with division of the ureter during excision of the rectum, we have recently reviewed the histories of 25 patients in whom such injury occurred during the course of 1611 operations for excision of the rectum for malignant disease at St. Mark's Hospital from 1940 to 1951 inclusive. These cases comprised both accidental and deliberate injuries, and included under the latter heading were 6 cases of complete pelvic clearance. In considering the management of these injuries 7 additional patients with ureteric section treated by one of us (J. C. G.) at St. Mary's or at St. Mark's Hospitals have also been studied. It is much to be regretted that fuller urological and biochemical investigation was not carried out on all these 32 cases post-operatively, but unfortunately several of them had succumbed in the immediate post-operative period or died subsequently of recurrence of malignant disease or other cause before this inquiry was inaugurated. Despite these omissions, however, certain points emerge regarding the incidence, prevention, and treatment of these injuries, and these will now be examined.

INCIDENCE

Accidental Injuries.—

Overall Incidence.—A total of 1605 patients were exposed to the risk of accidental ureteric damage, and 15 ureters were divided in 14 patients, giving a total incidence of injury of 0·93 per cent.

Sites of Injury.—The situations in which these ureteric injuries occurred are indicated in *Table I*,

Table I.—SITES OF ACCIDENTAL URETERIC INJURY DURING EXCISION OF RECTUM

SITES OF INJURY	NUMBER OF INJURIES	
	Left Ureter	Right Ureter
At level of ligature on inferior mesenteric vessels	2	—
At or just above the level of lateral ligament of rectum	7	6
All sites	9	6

from which it would appear that the ureter is equally liable to be divided on either side below the brim of the pelvis. Above the pelvic brim an additional hazard for the left ureter is represented by the main ligature on the inferior mesenteric vessels, for in two cases in this series the left ureter was caught up in this ligature and divided. The right ureter lies farther away from the mesenteric vessels, which incline somewhat to the left of the midline, as *Fig.* 180 shows, and this accounts for the immunity which the right ureter apparently enjoys from injury at this level.

Incidence of Injury relative to the Site and Extent of Growth.—Ureteric injury occurred with growths

in all situations in the rectum and rectosigmoid, as is indicated in *Table II*. As might have been expected, the growths which were complicated by injury to a ureter were usually adherent and presented technical difficulties to the surgeon, but in 2 of the

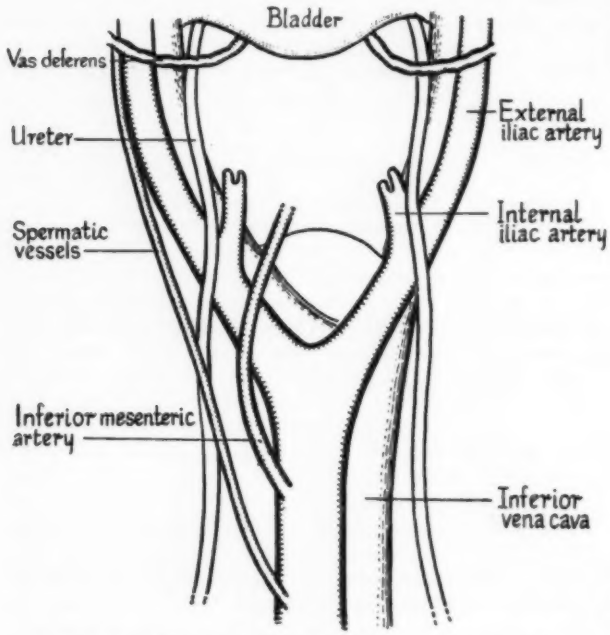

FIG. 180.—Diagram showing the relations of ureters to the inferior mesenteric, iliac, and spermatic vessels, and to the vasa deferentia.

14 patients the lesion was mobile. One of these patients was very obese, however, and the other had had a previous hysterectomy for carcinoma of the cervix which left much scar tissue enveloping the lower ends of the ureters.

Table II.—SITES OF CARCINOMA IN BOWEL IN CASES OF URETERIC INJURY DURING EXCISION OF RECTUM

SITE OF GROWTH	NO. OF URETERIC INJURIES
Rectosigmoid	2
Upper third of rectum	5
Middle third of rectum	5
Lower third of rectum	2
Upper third and lower third of rectum (double growth)	1
All sites	15

Incidence of Injury relative to the Type of Operation performed.—Table III shows the types of operation performed in this series. Though injury followed each of the three main forms of rectal excision employed—namely, the synchronous combined excision, the perineo-abdominal excision, and the anterior resection—it was in association with the first that most of the injuries occurred, and the relative incidence with it was much higher than with the other procedures. As the figures stand they seem to indicate that the ureters are less liable to be injured during a perineo-abdominal excision than an anterior resection or synchronous combined excision. It must be borne in mind, however, that one of the main advantages claimed for the synchronous combined excision is that it permits of excision of adherent growths which might be found inoperable by other methods, and it might be argued that the series of cases treated by synchronous combined excision probably includes an unduly high proportion of fixed growths which would render a fair comparison of the risk of ureteric injury with

Table III.—INCIDENCE OF URETERIC INJURY RELATIVE TO THE TYPE OF RECTAL EXCISION PERFORMED

TYPE OF OPERATION	NO. OF CASES TREATED	NO. OF URETERS INJURED
Synchronous combined abdomino-perineal excision	838	13
Perineo-abdominal excision	498	1
Anterior resection	135	1
Abdomino-anal excision	20	—
Hartmann's operation	18	—
Miles' operation	12	—
Total colectomy and synchronous combined excision	3	—
Total colectomy, rectal excision, and ileo-rectal anastomosis	1	—
Perineal excision	80	—
Total	1605	15

the different techniques of rectal excision mentioned impossible. So far as we can judge from examination of the case notes, there does not appear to have been any very marked difference in the mode of selection of cases for the perineo-abdominal and the synchronous combined excision respectively, though the anterior and abdomino-anal resections have only been applied to growths situated above a level 10 cm. from the anus. We are therefore of the opinion that the difference in the incidence of ureteric injury with different operations revealed in *Table III* does indicate that in general the ureters are less endangered by the perineo-abdominal than by the synchronous combined technique of rectal excision. This greater immunity is presumably related to the fact that in the perineo-abdominal operation the greater part of the dissection is carried out from the perineum, and in this connexion it is interesting to note that only one of the 15 accidental ureteric injuries in this series was produced during the perineal phase of the operation.

Deliberate Resections of the Ureter.—There were 11 patients in whom division of the ureter or ureters was carried out intentionally as part of a planned ureteric resection. Of these 11, 6 were cases submitted to complete pelvic clearance, in which the lower ends of both ureters were resected, together with the other pelvic viscera. The remaining 5 were cases in which a varying length of the lower end of one ureter was resected because of its involvement in the disease. All were patients in whom there was extensive local spread of carcinoma of the rectum but little or no evidence of the disease outside the pelvis.

PREVENTION OF ACCIDENTAL INJURIES

In the light of the information given in *Table III* regarding the incidence of accidental ureteric injury relative to the type of operation performed, an

obvious safeguard so far as the ureters are concerned would be to employ the perineo-abdominal technique to the exclusion of all others! Each method of rectal excision, however, has its respective advantages and disadvantages and its special indications, a discussion of which would be outside the scope of this paper, and it is probable that the majority of operations for carcinoma of the rectum will continue to be other than perineo-abdominal excisions. The remarks which follow regarding the avoidance of accidental injury to the ureters during excision of the rectum apply essentially to operations in which the dissection is largely or entirely done through the abdomen.

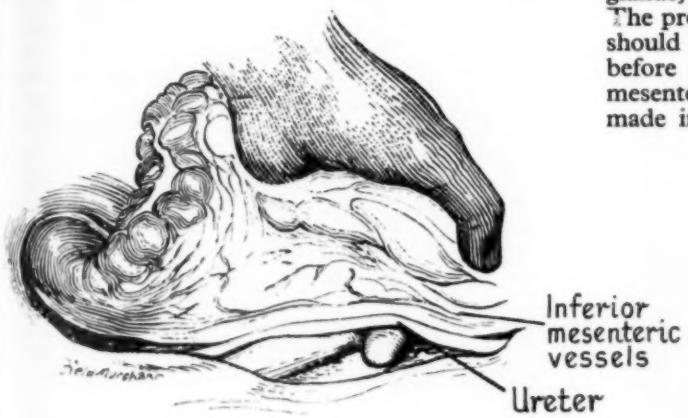

FIG. 181.—Diagram to show the danger of hooking up the left ureter in defining the inferior mesenteric vessels for ligation. The surgeon's finger has been passed from the right side under the base of the mesocolon and has inadvertently included the ureter along with the vascular pedicle.

Injury to the Left Ureter during Ligation of the Inferior Mesenteric Vessels.—As has been pointed out, this danger arises from the extremely close proximity of the left ureter to the inferior mesenteric trunk, the interval between being often only ½–¾ in. for 2 in. or so of their course (*Fig.* 180). If the surgeon is not careful, therefore, he may easily hook up the left ureter as he passes his finger under the superior vascular pedicle and proceed unconsciously to ligate and divide it (*Fig.* 181). If the pedicle should be bulky with fat or enlarged glands, this is perhaps even more likely to occur. The precaution that is required is that the left ureter should be carefully defined in this part of its course before any attempt is made to tie the inferior mesenteric vessels. It is identified as the cut is made in the peritoneum along the left side of the base of the sigmoid mesocolon and mesorectum, and it is then firmly pushed laterally and backwards for 3–4 in. of its course, to take it well away from the main mesenteric vessels (*Fig.* 182).

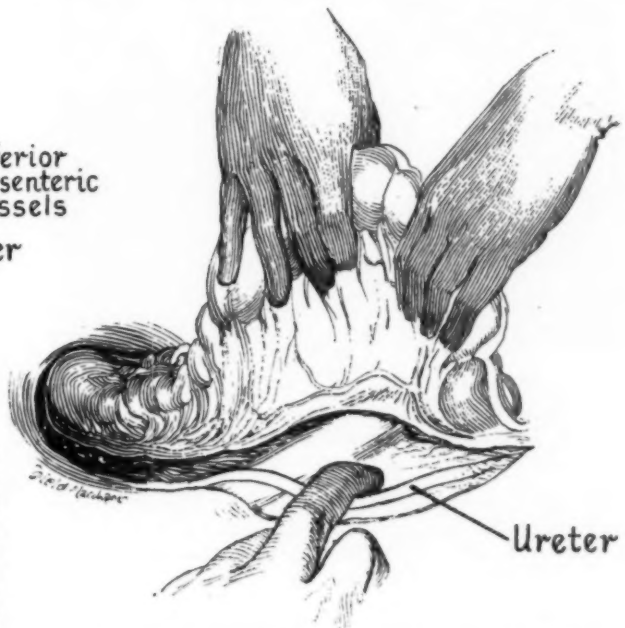

FIG. 182.—Separation of the left ureter from the inferior mesenteric vessels preparatory to ligation of the latter. The surgeon pushes the ureter firmly backwards for several inches with his finger to carry it away from the vascular pedicle.

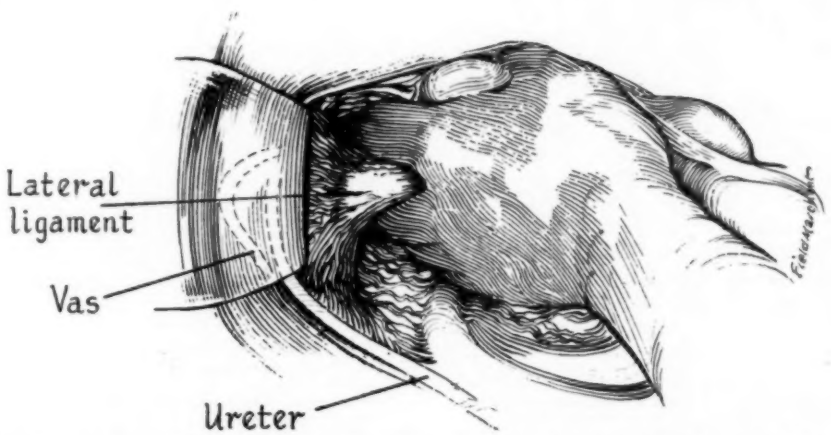

FIG. 183.—Division of the lateral ligament. The left ureter and vas have been strongly retracted by a deep pelvic retractor and the ligament has been defined between two fingers, ready for division.

Injury to Either Ureter during Division of the Lateral Ligament.—As regards the danger to the ureter during division of either lateral ligament,

this can only be avoided if the ureter is retracted lateral to the point of section of the ligament. In a case with a non-adherent growth it may be possible to do so blindly by retraction of the peritoneum and connective tissue in this region, but the only absolutely reliable method is to expose the ureter from the brim of the pelvis down almost to the bladder to ensure that it is accurately hooked aside by the retractor (*Fig.* 183). When the growth is extensive it may be found that the ureter is drawn medially by adhesions and that a determined dissection is necessary to separate it. In some cases it will be found that the ureter is so stuck to the neoplasm that it may be considered to be invaded by it, and

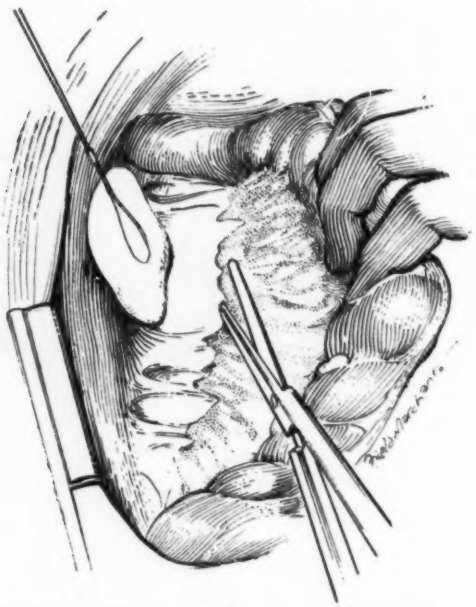

FIG. 184.—Division of the developmental adhesions on the left side of the iliac colon. This step mobilizes the colon and is an essential preliminary to accurate division of the peritoneum on either side of the base of the sigmoid mesocolon and mesorectum.

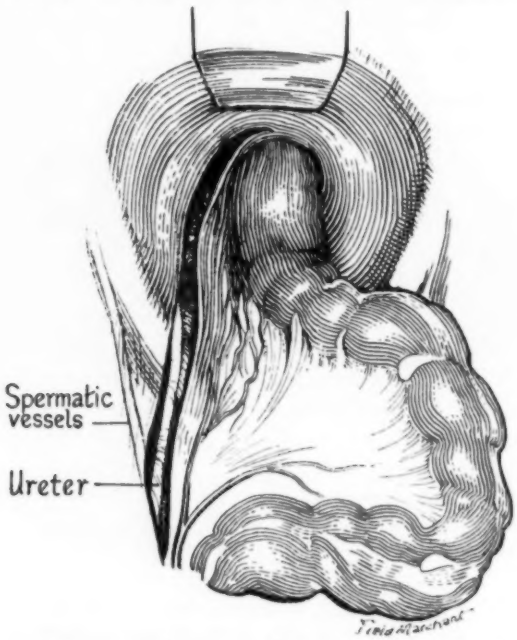

FIG. 185.—Exposure of left ureter by incision of peritoneum on the left side of the base of the mesosigmoid and mesorectum. The peritoneal cut has been carried forwards on to the base of the bladder.

FIG. 186.—Incision of peritoneum on the right side of the mesosigmoid and mesorectum in a female patient. Note that this does not immediately expose the right ureter, which lies more laterally under cover of the peritoneum, through which it and the ovarian vessels may be faintly outlined in thin subjects.

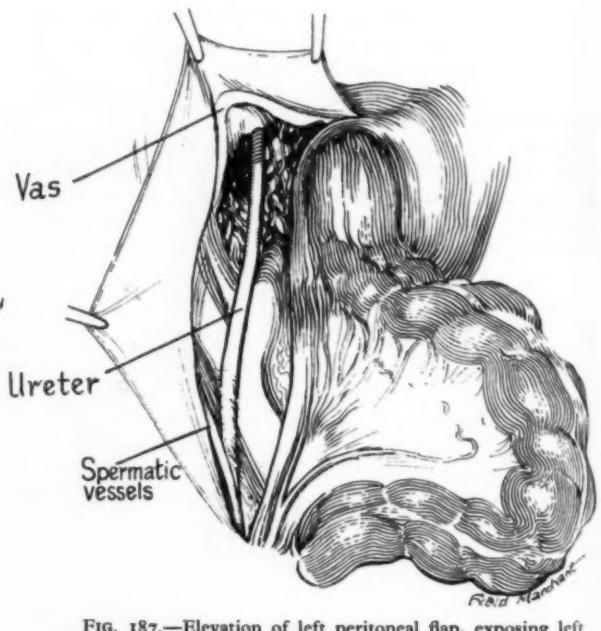

FIG. 187.—Elevation of left peritoneal flap, exposing left ureter throughout its course from the brim of the pelvis almost to the bladder. Note close relationship of the upper part of the ureter to inferior mesenteric and spermatic vessels and the crossing of its lower end by the vas deferens drawn up as a loop attached to the peritoneum. It will be observed that the ureter lies on the bifurcation of the common iliac artery.

the decision taken to resect 2–3 in. of it along with the rectum.

We have been so impressed with the desirability of identifying the ureters during excision of the rectum that we have made it our practice to expose both ureters throughout their pelvic course as an essential preliminary to dissection of the actual growth. The ureteric dissection is carried out after the iliac colon has been freed by scissor dissection of the developmental adhesions on its outer side (*Fig.* 184) and the peritoneum has been incised along either side of the base of the sigmoid mesocolon and mesorectum (*Figs.* 185, 186). The lateral peritoneal flaps are then elevated to a width of 3–4 in., exposing the ureter on either side where it crosses the bifurcation of the common iliac artery and tracing it downwards along the brim and side wall of the pelvis (*Figs.* 187, 188). The raising of the pelvic peritoneal leaves in this way is not an otherwise unnecessary

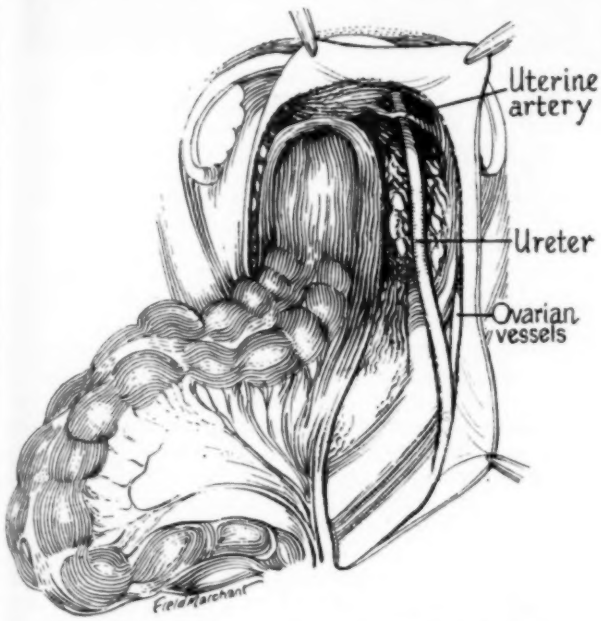

FIG. 188.—Elevation of right peritoneal flap in a female patient, exposing the ureter almost down to the bladder and showing the uterine artery crossing it near its lower end.

step because it would usually be required before suture of the pelvic peritoneum at the conclusion of the operation. Performed at this early stage it permits of accurate and efficient retraction of the ureters during the subsequent excision of the rectum, and incidentally encourages a wide removal of lateral ligaments along with the bowel (*Fig.* 183).

TREATMENT OF ACCIDENTAL INJURIES AND DELIBERATE RESECTIONS OF THE URETER

In the case of one of the accidental injuries (J. S., S.M.H. 27666), the method of treatment was not clearly indicated. The patient died five weeks after the injury and no autopsy was obtained. The treatment given to the other 13 patients in whom 14 ureters were accidentally injured, and to the 11 patients in whom part of one or both ureters was deliberately resected, will be considered together because the problem presented by both forms of injury is similar except for the fact that after deliberate resection end-to-end anastomosis is rarely possible. In addition, 2 cases of accidental injury and 5 cases of deliberate resection of the ureter during excision of the colon and rectum, dealt with by the senior author at St. Mary's or at St. Mark's

FIG. 189.—Intravenous pyelography on a patient with a urinary fistula four weeks after ligation of the left ureter, which was accidentally divided during combined excision of the rectum. Note the slight dilatation of the calices of the left kidney.

Hospitals, will also be included in our consideration of treatment. In all, then, the management of 31 patients will be considered. The methods of treatment used were as follows :—

1. Simple ligature of both cut ends of the ureter, 8 ureters.
2. End-to-end anastomosis of the ureter at the site of section, 6 ureters.
3. Suture of a partially divided ureter, 2 ureters.
4. Substitution of a segment of ileum for a resected segment of ureter, 3 ureters.
5. Implantation of the proximal cut end of a ureter into the bladder, 4 ureters.
6. Implantation of the proximal cut end of a ureter into the colon, 10 ureters.
7. Cutaneous ureterostomy, 1 ureter.
8. No treatment, 1 ureter.

1. Simple Ligature of Both Cut Ends of the Ureter.—Eight ureteric injuries which all occurred during rectal excisions by the synchronous combined method were treated in this way. One patient died during the period of post-operative hospital stay. This death occurred on the forty-ninth post-operative day from uræmia. A number of factors contributed to the terminal uræmic state, chief among which were cardiac failure, bronchopneumonia, and an infected hydronephrosis on the side of the tied ureter.

The 7 cases which survived operation progressed as follows :—

a. Five developed urinary fistula from the divided ureter. In 3 of these cases the leak was from the perineal wound and manifested itself from two to three weeks after operation. All three cases were submitted to nephrectomy and all recovered. Only one of the excised kidneys was described. It showed " a moderate degree of hydronephrosis, with grossly infected urine in the pelvis ". The

intravenous pyelogram in this case is reproduced in *Fig.* 189.

In the other two cases the leak was into the abdominal cavity and presented as an abdominal swelling. In one " an enormous enlargement of the kidney " was diagnosed clinically four months after the ureter on that side had been tied. Operation showed that this swelling in the loin was, in fact, an extraperitoneal collection of urine coming from the ureter at the site of ligature. Nephrectomy was performed and recovery occurred. The kidney was macroscopically normal. The other case returned with a lower abdominal swelling seven weeks after a ureteric tie. Laparotomy showed that this consisted of an encysted intraperitoneal collection of urine lying in relation to the site of ureteric injury. Recovery followed nephrectomy, again with removal of an apparently normal kidney.

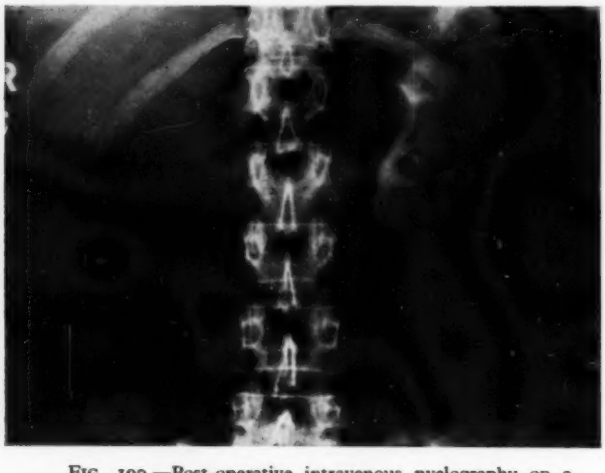

FIG. 190.—Post-operative intravenous pyelography on a patient three months after end-to-end anastomosis of the right ureter following combined excision of the rectum with partial ureteric resection. Note the failure of excretion of the contrast medium on the right side, indicating non-function of the right kidney. The soft-tissue shadow of the right kidney is clearly defined and does not appear enlarged.

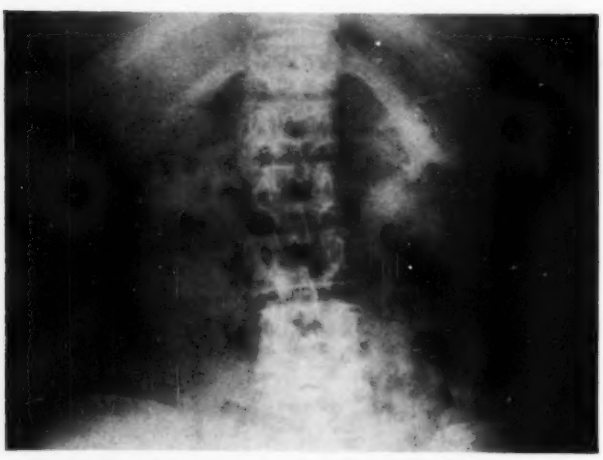

FIG. 192.—Intravenous pyelography two months after end-to-end anastomosis of the right ureter following excision of a rectosigmoid carcinoma with partial ureteric resection. The radiologist reported delay in excretion from the right kidney and the ill-defined right pyelogram shows some degree of dilatation of the calices.

Regarding the ultimate fate of these 5 cases, 2 patients seen in the third and fourth years after nephrectomy were well and apparently free from malignant disease; 2 patients developed recurrence of the cancer in the perineum in the third and fourth years respectively after nephrectomy; whilst 1 patient was found to have hepatic metastases twenty-two months after operation.

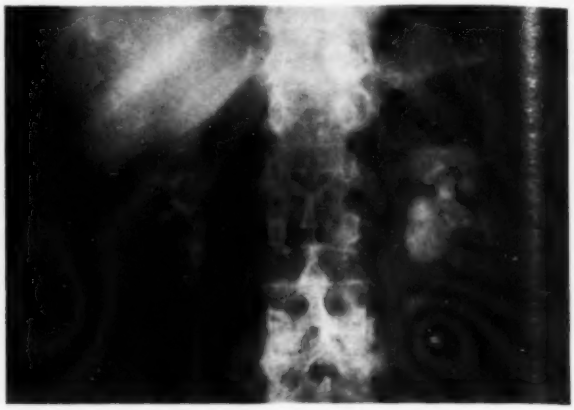

FIG. 191.—Post-operative intravenous pyelography on a patient two weeks after end-to-end anastomosis of the left ureter following colectomy with accidental ureteric division. Note the mild degree of hydronephrosis and hydro-ureter revealed on the left side, but the good excretion of dye, indicating excellent renal function. At this stage the patient had a urinary fistula from which all the urine from the left kidney was escaping. The pyelogram of the right kidney appears perfectly normal.

b. In 2 cases tying of the ureter as a method of treatment for its section was clinically successful. One of these cases died from recurrence of the malignant disease one year after excision of the rectum. The other case was reported alive and well six years after the rectal excision. No fistula had developed in either case. No loin pain was complained of and no hydronephrosis was detected clinically.

Unfortunately there is scant information about the type of ligature material used in the tying of the above ligatures. In some cases the records indicate that the ureter was ' doubly tied ' (probably with linen thread).

2. End-to-end Anastomosis of the Ureter at the Site of Section.—In 5 patients 6 cut ureters were treated in this way. Not one case was successful. The record of these cases is as follows :—

a. W. I., S.M.H. 51694.—Both ureters were accidentally divided near the pelvic brim during synchronous combined excision of the rectum for a large, fixed growth in its middle third. End-to-end anastomosis of both ureters was carried out over ureteric catheters, using interrupted catgut sutures. Urine drained from these catheters for one day only. Thereafter all urine came through the perineal wound. This patient died eleven days after operation in diabetic pre-coma. Necropsy showed abscesses at sites of ureteric anastomosis.

b. Mrs. H. P., S.M.H. 41026.—The left ureter was divided by the perineal operator during a synchronous combined excision of the rectum. The growth was one in the upper third of the rectum and it had spread extensively into the left lateral

ligament. End-to-end suture of the ureter was carried out. The patient died of ' shock ' two hours after operation.

c. Miss D. M., St. Mary's Hosp. 357377.—Deliberate resection of about 1 in. of the right ureter, together with the uterus and rectum for an extensive rectal carcinoma. The continuity of the right ureter was restored by end-to-end anastomosis over a ureteric catheter, using interrupted catgut sutures. There is no record as to whether this catheter ever discharged any urine before it was withdrawn on the ninth post-operative day. For about two months after operation the patient had pain in the right loin. An I.V.P. (*Fig.* 190) three months after operation was reported on as follows: " At no stage up to one hour is there any radiological evidence of renal function on the right side." The patient unfortunately succumbed from recurrence two months later; no necropsy was obtained.

d. Mrs. M. A. W., St. Mary's Hosp. Y4482.—The left ureter was accidentally divided in its abdominal course during the performance of a left hemicolectomy for carcinoma. End-to-end anastomosis of the ureter with four interrupted catgut sutures was carried out. A catheter could not be passed to act as a splint for the anastomosis. A persistent urinary fistula developed and an I.V.P. showed a left hydronephrosis (*Fig.* 191). Nephrectomy was performed three weeks after the first operation.

e. Mrs. A. G., St. Mary's Hosp. 357864.—In this case a carcinoma of the sigmoid colon was present. One inch of the right ureter was intentionally resected together with sigmoid colon. Continuity of the ureter was restored by anastomosis over a ureteric catheter. Interrupted ' deknatel ' sutures were used for the anastomosis. There is no record as to whether this catheter discharged any urine up to the time of its withdrawal on the tenth post-operative day. Two weeks after operation an intravenous pyelogram showed some renal function on the side of the anastomosis. Two months later there was a large fluctuant swelling in the right loin and evidence of impaired kidney function on that side (*Fig.* 192). An incision into the swelling showed that it consisted of extravasated urine, which was apparently coming from a large defect in the ureteric anastomosis. Right nephrectomy was performed. This kidney was normal in size. There was mild chronic inflammatory change in the pelvis and ureter.

3. Suture of a Partially Divided Ureter.—This was done in 2 cases. One was followed up for only two months after the injury and received no urological investigation apart from urine examination. There was no clinical evidence to suggest that the ureteric injury had produced ill effects. This particular case was the only one in the whole series of ureteric injuries which occurred during rectal excision by the perineo-abdominal method. The other case died twenty-five days after operation. Death was due to pelvic sepsis produced, it was thought, by perforation of the bladder with a urethral catheter. Post-mortem examination of the kidney on the side of ureteric injury showed that its pelvis was dilated and contained foul pus. The other kidney appeared normal.

4. Substitution of a Segment of Ileum for a Resected Segment of Ureter (*Fig.* 193).—This was carried out on 3 occasions. All three cases must be regarded as failures. Their records are as follows:—

a. Mrs. L. M. G., S.M.H. 47986 (*aged* 62).—A difficult synchronous combined excision of the rectum, which was combined with hysterectomy because of local spread of the rectal growth. During

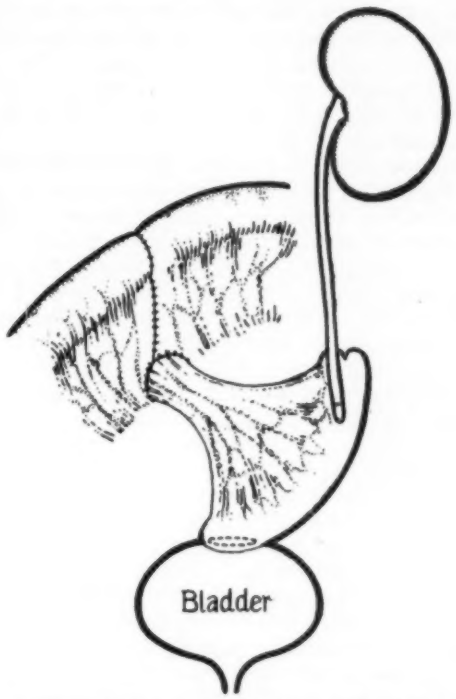

FIG. 193.—Diagram of the technique employed to replace the lower part of the ureter by a loop of ileum isolated except for its blood-supply.

dissection it was realized that the right ureter had been endangered, but no definite evidence of injury to it was seen. Three weeks after this operation a perineal urinary fistula was diagnosed. A laparotomy confirmed that this derived from the right ureter. This ureter was divided, above the fistula, and an isolated segment of ileum was anastomosed at one end to the bladder and at the other to the proximal cut end of the ureter. Subsequently the patient did well at first, and had no further leakage of urine. Unfortunately, she persisted with gross sepsis in the urinary tract, and it was eventually decided that this would not clear up till the artificial ureter was removed. Accordingly, six months after operation right nephro-ureterectomy and excision of the isolated piece of ileum were performed. The kidney showed gross hydronephrosis and infection and the ' ileal ureter ' was greatly dilated. The patient died three weeks after the nephrectomy from retroperitoneal infection.

b. Mrs. E. H., St. Mary's Hosp. 312345 (*aged* 58).—This patient had a large carcinoma of the rectum for which a Hartmann type of operation was performed and was extended to include hysterectomy and partial right ureterectomy because of involvement of uterus and ureter by the growth. The

continuity of the ureter was restored, as in the above case. The total operating time was 3½ hours. Death occurred on the eighth post-operative day. Cause of death was given as " extrarenal azotæmia due to paralytic ileus ". The pathologist reported further that " all anastomoses were sound ".

c. Mrs. M. H., St. Mary's Hosp. 332012 (*aged* 42).—The sigmoid colon, the uterus, and part of the left ureter were excised *en bloc* for a carcinoma originating in the sigmoid colon. An isolated loop of ileum was fashioned and arranged as a substitute for the resected ureter, as in the above two cases. Total operating time was 3 hr. 50 min. The patient died two days after operation from bronchopneumonia and thrombosis of the left common iliac artery, again all anastomoses being intact.

5. Implantation of the Proximal Cut End of a Divided Ureter into the Bladder.—This procedure was carried out on 4 occasions. All four were cases in which ureteric section had been made at the level of the lateral ligament of the rectum. The technique of implantation was usually that of Marion (1935). Only one of these patients had cystoscopic examination or urography post-operatively. These were carried out a year after operation because of the sudden onset of urinary symptoms and revealed a bladder stone which was treated by crushing. On the whole the four cases did well, as regards their urinary tracts, so far as could be judged clinically. Only one of them developed a urinary fistula after operation and this cleared up after a week. None of them required subsequent nephrectomy during the period of follow-up. Three of these patients complained of varying degrees of dysuria after discharge from hospital. One has been mentioned above. The other two reported themselves as having occasional frequency and scalding. Three of these cases died of metastases of the rectal growth within twenty months of their operations. One case could only be followed up for a year after operation and was then well.

6. Implantation of the Proximal Cut End of a Ureter into the Colon.—This method of disposal of the divided ureter was used in 5 cases undergoing complete pelvic clearance, where of course both ureters were implanted and in 2 cases treated by anterior resection, in each of which the ureter was divided or resected. In one case of pelvic clearance the ureters were implanted separately into the colon, just above a left iliac colostomy, by a Coffey I technique. In this case a transverse colostomy had previously been established, and from this the fæces continued to discharge, while the urine was collected into a ' stick-on ' type of ileostomy bag in the left iliac fossa. This patient remained well for five months after this operation and then showed evidence of recurrence of the cancer at the left iliac colostomy. No urography was carried out. A second case had the ureters implanted into the cæcum, after ' gun-barrelling ', by a Coffey I technique. Intravenous pyelography five weeks after operation showed normal function and anatomy in both kidneys. The patient lived for seventeen months subsequently; death, according to the report submitted by the hospital where it occurred, was due to " toxæmia associated with perinephric abscess ". This abscess was drained shortly before death. Apparently no post-mortem examination was carried out. Of the other two cases, one died on the seventh post-operative day of cardiovascular collapse, precipitated by intestinal obstruction; the other died on the twentieth day after operation from thrombosis of both common iliac veins. Both had ureteric implants into the cæcum. In both cases post-mortem examination showed that the ureteric implants were satisfactory and that in one case the kidneys were normal. The kidneys of the other showed congestion and œdema but were otherwise normal. The fifth case of pelvic clearance died on the operating table as the ureters were about to be implanted into the bowel.

Two cases had one ureter implanted into the bowel above an anterior resection anastomosis. The outcome in both these cases was satisfactory. The follow-up period in both cases was fairly short, however. Operations and progress were as follows :—

a. T. P., S.M.H. 50241.—This man was 61 years old when a restorative resection of the sigmoid colon was carried out for carcinoma. Because of involvement in the growth, part of the left ureter was resected. The proximal remaining segment of the ureter was implanted into the colon, proximal to the anastomosis, by a Coffey II technique. The immediate post-operative progress was satisfactory and ten months later there was complete rectal continence. At that time urine was being passed from the rectum about every two hours. Intravenous pyelography a month after operation revealed some hydronephrosis on the side of the ureteric implantation and a repeat examination six months later shows that this is unchanged.

b. Mrs. R. L., St. Mary's Hosp. 322051.—This patient, aged 62, had a restorative resection of the sigmoid colon for a mass (subsequently shown to be inflammatory) arising from the colon at the recto-sigmoid junction and involving the left ureter. The involved segment of ureter was resected with the colon and a Coffey II technique was used to unite the proximal ureteric segment to the colon above the anastomosis. When she left hospital three-and-a-half weeks later she had normal rectal control and was passing urine per anum about every three or four hours. Intravenous pyelography then showed a moderate degree of hydronephrosis on the affected side. When seen four months later her frequency had diminished somewhat and radiological examination revealed no change in the condition of the left kidney.

7. Cutaneous Ureterostomy.—This was carried out in 1 case of pelvic clearance. This patient only possessed one kidney and its ureter was brought to the skin surface. It discharged urine satisfactorily until the tenth post-operative day, when the patient died from paralytic ileus. Post-mortem examination showed that the single kidney was large in size but was otherwise normal.

8. No Treatment.—In 1 patient the right ureter was accidentally divided during a synchronous combined excision for a carcinoma of the middle third of the rectum which had spread extensively into the pararectal tissues. The section was situated immediately below a segment of ureter which appeared to be completely blocked by growth. This patient died

three months after operation from " carcinoma of the rectum ". She developed no signs or symptoms due to the obstruction of her ureter.

DISCUSSION

A consideration of the foregoing experiences in the management of ureteric injuries permits certain conclusions to be drawn regarding the efficacy of the different methods employed. Though the relevant urological data are not complete, the technique which appears to emerge with greatest credit is that of *implantation of the upper end of the ureter into the bladder*. This has the advantages of restoring to the patient a substantially normal urinary tract and avoiding fistulæ or disturbing urinary symptoms. Unfortunately it can only be adopted when the ureteric injury is situated low down in the pelvis, usually where the lateral ligament of the rectum is divided. We are of the opinion, however, that in every case of fairly low ureteric injury or resection it is the surgeon's duty to test the possibility of implanting the proximal portion of the ureter in the bladder before contemplating any alternative disposal. As regards the technique of uretero-cystostomy, the four vesical implants in this series were all done by the method usually associated with the name of Marion (1935).

It is only in cases with ureteric injuries too high to permit of the establishment of uretero-cystostomy, or where the bladder has had to be sacrificed as in a complete pelvic clearance, that the surgeon need consider alternative methods of dealing with the ureter. If the bladder has been retained and the level of the ureteric injury (or injuries) renders uretero-cystostomy impossible, the surgeon may still be tempted to conserve the affected kidney and to try to restore the continuity of the urinary tract, as was done in 9 of our cases of ureteric injury by end-to-end anastomosis of the ureter over an indwelling ureteric catheter in 6, and by sacrificing the distal ureteral segment and manufacturing a new lower ureter out of an isolated segment of ileum in 3 cases. It should be noted, however, that in none of these cases was a successful result obtained. Two of the patients treated by ureteric anastomosis succumbed within a few days of operation so that the success of the ureteric suture could not be properly assessed, but all the other cases treated in this way were complicated by the development of persistent urinary fistulæ or were followed by complete failure of renal function on that side or by hydronephrosis and infection. Even suture of a partially divided ureter, which was performed in 2 cases, was followed by dilatation and infection in 1 case.

These results with ureteric suture are disappointing in view of the successes claimed by Millin (1949) for this procedure.* So far as we can gather, the technique of anastomosis employed in our cases did not differ essentially from that recommended by Millin—namely, direct approximation by four or five interrupted sutures of fine plain catgut over an indwelling ureteric catheter or rubber tube. The possibility that other techniques for ureteric anastomosis might yield better results certainly requires to be explored. Moore (1948) has pressed the merits of an end-in-end anastomosis of the ureter instead of the more conventional end-to-end, but the reports on his cases treated in this way make it difficult to evaluate the results. Newell (1939) has established a temporary ureterostomy proximal to an end-to-end anastomosis by bringing out a ureteric catheter through an opening in the wall of the ureter to the skin surface, but again it is difficult from his paper to determine how successful his cases were as regards kidney function and avoidance of fistula formation, hydronephrosis, or infection. Finally, in experimental surgery in the dog, direct anastomosis of a divided ureter using a very fine silk technique is apparently capable of giving good union without leakage (personal communication from W. J. Dempster). Various methods of reinforcing a ureteric anastomosis by wrapping peritoneum, fascia lata, or an autogenous vein graft around it or by burying it with Lembert sutures in a loop of small intestine readily come to mind, and it seems possible that a more satisfactory method of anastomosis might be worked out on the basis of experimental work. But till this has been done, direct suture of a divided ureter must be regarded as an unreliable method which will very probably result in failure. Under the circumstances we cannot at present recommend its employment in the management of these injuries.

The method of making a new lower ureteric segment out of an isolated piece of ileum, though found to be eminently satisfactory in experimental work in dogs by Annis (1952) and Davids and Lesnick (1953), was unsuccessful when used in practice by us. In our experience the manufacture of an intestinal ureter in this way takes over an hour to perform, so that it represents a not inconsiderable addition to an already prolonged rectal excision. It is not perhaps surprising to learn that two of our three patients subjected to this form of ureteroplasty died within a few days of operation of extrarenal azotæmia secondary to paralytic ileus and to bronchopneumonia respectively; at autopsy the suture lines were all intact. The third case, which survived for six months, developed persistent urinary sepsis and gross dilatation of the renal pelvis, ureter, and intestinal ureter on the affected side, a complication which did not occur in Annis's experimental animals. Our experiences with this method, though too small to be conclusive, are certainly not very encouraging.

If, as seems to be the case, restoration of continuity is not really practicable in dealing with higher ureteric injuries, the kidney function on that side may still be conserved by implanting the ureter into the intestine or bringing it out to the skin surface as a cutaneous ureterostomy. When the bladder has had to be removed, as in cases treated by complete pelvic clearance, either of these procedures must of necessity be employed on both sides—bilateral intestinal implants or bilateral ureterostomies. Occasionally, as in two of our cases, where a high ureteric resection had to be carried out on one side in conjunction with an anterior resection of the rectum for carcinoma, it may be found possible to implant the proximal end of the ureter into the

* Through the courtesy of Sir Heneage Ogilvie we have recently seen a patient of his who had had a ureteric resection with end-to-end anastomosis in conjunction with a colectomy some eight years previously, and who now shows a perfectly normal pyelogram and ureterogram on that side.

colon above the bowel anastomosis so that the anal sphincters can be used to control the escape of urine and avoid urinary incontinence. More frequently, however, the entire rectum and sphincter apparatus has had to be removed and a colostomy established, so that implantation of the ureters into the right or left colon results in a wet colostomy which calls for special management with a stick-on type of ileostomy bag. To lessen the risk of ascending urinary infection from the colon and absorption of urinary chloride from the bowel with resulting production of hyperchloræmic acidosis, the alternative procedure of implanting the ureter or ureters into an isolated, short segment of cæcum and ascending colon, or, better, ileum as recommended by Bricker (1950) may be adopted, but these portions of bowel then drain urine to the surface as a cæcostomy or ileostomy, and require the same sort of management with an adhesive appliance. If, instead of implanting the ureters into the bowel a cutaneous ureterostomy (or ureterostomies) is established, similar problems in post-operative management arise, but it is especially difficult to keep ureterostomy patients dry by any form of appliance.

Where the bladder has been removed in a complete pelvic clearance and both ureters have to be disposed of, some one of these methods must be employed—preferably implantation into a short ileal segment—and the resulting inconvenience accepted. But when the division of the ureter is unilateral and the opposite kidney and ureter and the bladder are intact, it seems to us that the surgeon should weigh up very carefully the possible inconveniences, in the form of wet colostomies, cæcostomies, or ileostomies—of conserving the kidney on the affected side. Undoubtedly most patients would prefer to be spared these disabilities and, provided the surgeon can feel a normal kidney on the opposite side, it is almost certainly quite safe to sacrifice renal function on the side of the divided ureter. We are therefore driven reluctantly to the conclusion that in many of these cases simple ligation of both cut ends of the ureter, preferably with double strands of linen or cotton thread, will be the most satisfactory course. As accidental ureteric division or deliberate ureteric resection are most likely to take place in cases in which the excision of the rectum is prolonged and difficult, a method which enables the surgeon to dispose of the urinary complication in this expeditious manner has an additional advantage. As regards the probable subsequent course after this procedure, our experiences with 8 cases treated by ligation of the ureter are particularly instructive. Nearly three-quarters of our cases had later urinary trouble in the form of urinary fistulæ from the ligated lower end, or hydronephrosis or infection, so that nephrectomy frequently became necessary. However, even if removal of the kidney is required later, the necessity for this step normally does not arise till some time after the main operation, when the patient is well able to stand a nephrectomy.

CONCLUSIONS

1. In the course of excision of the rectum the ureter may be damaged on either side when the lateral ligament is being divided, and on the left side in addition when the inferior mesenteric vessels are being tied. The injury seldom occurs during the perineal phase of the dissection and possibly for that reason is extremely rare with the perineo-abdominal operation in which the bulk of the dissecting is done from below.

2. To avoid ureteric injury during rectal excision by other than the perineo-abdominal technique, it is recommended that as the first step in the pelvic dissection both ureters should be demonstrated throughout their course and the left one separated from the inferior mesenteric vessels; this allows them freely to be retracted at all stages of the operation.

3. It is recognized that occasionally the ureter is implicated in the growth; deliberate resection of the affected ureteric segment may then be necessary.

4. In the treatment of divided ureters, methods of direct anastomosis of the two parts of the ureter or of the manufacture of an 'intestinal' ureter out of ileum to convey the urine to the bladder have not been successful.

5. Wherever possible in such cases a ureterocystostomy should be performed. If the ureteric injury is too high to permit of this the divided end of ureter may be implanted into the colon or into an isolated short segment of ileum, but, as this will usually result in a 'wet' colostomy or ileostomy, it is preferable—provided the opposite kidney is normal on palpation—to carry out ureteric ligation. The consequence of this step in the majority of instances will be that a urinary fistula, hydronephrosis, or renal infection will develop later and require nephrectomy.

6. When pelvic clearance is carried out the best disposal of the ureters would appear to be to implant them into an isolated piece of ileum, the end of which drains to the surface as a urinary ileostomy.

We wish to record our thanks to our surgical colleagues at St. Mark's Hospital for permission to include their patients in this analysis; to Dr. Rohan Williams for the radiographs shown in *Figs.* 190–193, and Dr. N. P. Henderson for that in *Fig.* 189; to Dr. P. N. Cardew for preparing these radiographs for reproduction; to Professor Newcomb and his assistants for the necropsy reports on two cases at St. Mary's Hospital; and to Dr. Cuthbert Dukes for similar information regarding seven cases at St. Mark's Hospital; to Mr. H. J. R. Bussey, B.Sc., for statistical data; and lastly to the British Empire Cancer Campaign for a grant which defrayed some of the costs of the inquiry.

REFERENCES

ANNIS, D. (1952), *Proc. R. Soc. Med.*, **45**, 483.
BRICKER, E. M. (1950), *Surg. Clin. N. Amer.*, **30**, 1511.
DAVIDS, A. M., and LESNICK, G. J. (1953), *Ann. Surg.*, **137**, 389.
MARION, G. (1935), *Traité d'Urologie*, 1013, Paris: Masson.
MILLIN, T. (1949), *Proc. R. Soc. Med.*, **42**, 37.
MOORE, T. D. (1948), *J. Urol.*, **59**, 712.
NEWELL, Q. U. (1939), *Ann. Surg.*, **109**, 981.

CHOLECYSTITIS AND CHOLELITHIASIS IN CHILDHOOD

By ISABELLA FORSHALL and P. P. RICKHAM, Liverpool

In October, 1721, Joseph Gibson, a surgeon in Leith, was called to see a boy 12 years of age complaining of right-sided abdominal pain. The patient developed a hectic temperature and vomited frequently; jaundice developed and the stools became white. During the next few months a large mass became palpable in the right hypochondrium. The child's condition slowly deteriorated, the abdomen was grossly distended, and two days before death, 12 lb. of turbid green fluid were removed by paracentesis. At autopsy " the gall-bladder extended to a most surprising bulk for it contained no less than two Scotspints, or eight pounds of bile ". (Gibson, 1734.)

Gall-bladder disease in childhood has been considered to be very rare, almost a pathological curiosity. It is therefore surprising that over 500 cases are recorded in the literature. Many of the cases published in the eighteenth and nineteenth century were, in fact, suffering from hepatitis or peritonitis. A critical survey of the literature by Ulin, Nosal, and Martin (1952) revealed 326 proved cases up to and including 1948. Six children submitted to operation for gall-bladder disease during the last five years are here reported.

CLINICAL FINDINGS

The more important clinical findings in our 6 cases are set out in *Table I*. Certain points, however, need some further observations.

Sex.—All our patients were girls. Gall-bladder disease in adults is much more common in females than males. Amongst children, however, males are more often affected than females, the boy : girl ratio being 3 : 2 (Ulin, Nosal, and Martin, 1951).

Age.—Our youngest child was 2½ years old; much younger patients have been reported in the literature. Booker (1952) and Snyder, Chaffin, and Oettinger (1952) successfully operated on children of 7 and 6 weeks of age respectively suffering from gall-bladder disease.

Signs and Symptoms.—Three of our cases were admitted as emergencies. *Case* 6 had suffered from symptoms for two years and was sent to hospital during an acute exacerbation. Only one patient (*Case* 1) was gravely ill on admission.

The symptoms of biliary disease in children are often vague; mild generalized abdominal pain, nausea, vomiting of stomach contents or more rarely bile-stained material, constipation, and headache, are the most common complaints. Pain in the back and shoulder, so common in adults, is very rare in childhood (Gross, 1953). None of our children gave a history of intolerance to fatty foods. Jaundice, a common accompaniment of gall-bladder disease in adults, was not seen in any of our cases. This is interesting, as the incidence of jaundice in children is higher than in adults (Ulin and others, 1952). Sobel (1938) has suggested that all cases of jaundice in childhood should have a Graham's test performed to exclude gall-stones. Clinical examination of the abdomen may be completely negative, but pain or guarding in the right hypochondrium is not uncommon. In only one of our cases was a positive Murphy's test elicited.

X-ray and Laboratory Investigations.—We have made a point of X-raying the abdomen of all children who suffer from undiagnosed recurrent abdominal pain, or who are sent to hospital with a tentative diagnosis of acute appendicitis and symptoms which quickly subside after admission, and agree with Ulin and others (1952) that in all children suffering from recurrent abdominal pain or dyspepsia it is important to exclude peptic ulcer and gall-bladder disease.

Fig. 194.—*Case* 3. Abdominal radiograph showing solitary radio-opaque shadow.

The diagnosis of gall-stones was made in 5 cases by a straight radiograph of the abdomen which showed one or more opaque shadows (*Figs.* 194, 195). A Graham's test was performed in all 5 cases; the dye was well concentrated in all but *Case* 6 (*Fig.* 196). A full blood investigation was performed in every case. With the exception of *Case* 1, which had a marked leucocytosis, nothing abnormal was discovered. The fragility test was normal in all patients. Liver function tests were performed in 4 patients and were within normal levels. The serum-cholesterol was estimated in 3 patients and was found to be normal.

TREATMENT

Cholecystectomy was performed in all our cases. In mild cases of cholecystitis medical treatment has a place, but in cases of cholelithiasis cholecystectomy is the treatment of choice. In some children with

gall-stones the gall-bladder appears quite normal and cholecystostomy has occasionally been recommended. We consider that this is a mistake, as even a normal-looking gall-bladder can be associated with an abnormal cystic duct, as will be shown later on.

FIG. 195.—*Case* 2. Abdominal radiograph showing four small radio-opaque shadows.

FIG. 196.—*Case* 5. Graham's test. The gall-bladder concentrates the dye well. There is a radio-opaque shadow in the gall-bladder.

Edington (1930) reported the case of a child on whom a cholecystostomy had been performed and who had to undergo a cholecystectomy several years later for recurrence of symptoms. In children with acute cholecystitis, where cholecystectomy can be very difficult because of gross œdema of the surrounding structures, Gross (1953) advises cholecystostomy as a safer operation. In *Case* 1 there was an enormous gangrenous gall-bladder, tensely distended with mucopus, and gross œdema of the lesser omentum; cholecystectomy was, however, performed without undue difficulty. An incision running obliquely downwards and medially from a point on the costal margin about 1 in. outside the nipple line for about 4 in. is very satisfactory for cholecystectomy in children; it gives a good exposure and runs in the same direction as the subcostal nerves.

POST-OPERATIVE PROGRESS

The literature suggests that surgery of biliary diseases is more straightforward in children than in adults (Ulin and others, 1952). All our children were discharged from hospital 10–14 days after operation and their subsequent progress has been satisfactory, except for *Case* 4. This girl's abdominal pain recurred following operation. Her home conditions were very unsatisfactory and it became apparent that the recurrence of symptoms had a psychological basis; she was referred to the child psychiatric clinic.

Table I.—DETAILS OF CASES OF GALL-BLADDER DISEASE

CASE	NAME	AGE	PRESENTING SYMPTOMS	DURATION OF SYMPTOMS	SIGNS	ADMISSION TO HOSPITAL	X-RAY FINDINGS	PATHOLOGY
1	Rosalind	2½ yr.	Abdominal pain	7 d.	Very ill, tenderness in R.I.F. T. 102°	Emergency	—	Gangrenous cholecystitis
2	Hilary	6 yr.	Abdominal pain and vomiting	5 mth.	—	For investigation	Opaque stones	4 pigment stones
3	Margaret	9½ yr.	Abdominal pain	4 d.	Guarding right hypochondrium	Emergency	Opaque stones	1 pigment stone
4	Marjorie	10 yr.	Abdominal pain and nausea	2 yr.	—	For investigation	Opaque stones	1 pigment stone
5	Barbara	10½ yr.	Abdominal pain and nausea	1 yr.	Murphy's sign positive	For investigation	Opaque stones	1 pigment stone
6	Marjorie	12 yr.	Bilious vomiting	2 yr.	Ill child; tender right hypochondrium	Emergency during acute exacerbation	Opaque stones	3 cholesterol stones

AETIOLOGY AND PATHOLOGY

A considerable amount has been written about the aetiology of gall-bladder disease in childhood and many causative factors have been suggested. In the majority of cases no cause or explanation for the development of gall-stones has been found. There is no doubt that hæmolytic jaundice predisposes to gall-stones (Gairdner, 1939). None of our cases has had acholuric jaundice and none of the cases of acholuric jaundice admitted to the three children's hospitals on Merseyside during the last five years have suffered from gall-stones.

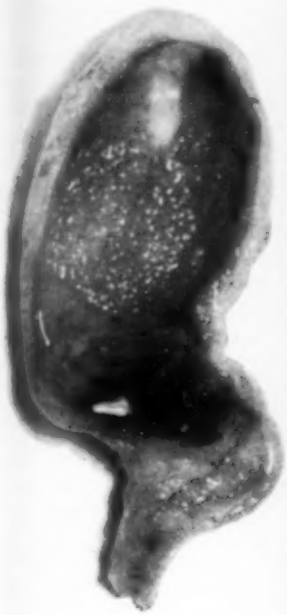

FIG. 197. *Case* 5. Specimen of gall-bladder with pigment tone lying in Hartmann's pouch.

FIG. 198.—*Case* 6. Specimen of chronically inflamed gall-bladder. A cholesterol stone is impacted in Hartmann's pouch.

FIG. 199.—Dissection of the cholecystic duct reveals another cholesterol stone embedded in a diverticulum (D) opposite to Hartmann's pouch (H). The cholecystic duct joins the gall-bladder at (E), winds around the diverticulum, and narrows at the stricture (S).

Various infections have been cited as causative factors. Typhoid fever in association with gall-stones has been reported; Reid and Montgomery (1920) collected 18 instances from the literature and a few further cases have been reported since then. Scarlet fever has also been blamed; Schottmueller (1931) collected 5 cases. Gall-stones are, in fact, a very rare complication of scarlatina. Swing and Bullowa (1919) found only 2 cases amongst 12,352 children suffering from scarlet fever. *Lamblia intestinalis* as a causative agent has been suggested by Lowenburg and Mitchell (1938), but the supporting evidence is very inconclusive. Bonta and Lovingood (1952) suggest respiratory infections, and point out that less children have been reported in the 1940/50 period than in the 1930/40 period; they believe that the advent of chemotherapy accounts for this decline.

Anatomical defects have seldom been postulated as a causal factor in cholecystitis. Jones (1951) reported the case of a girl of 3 years of age with acute cholecystitis due to an enlarged cystic gland blocking the cystic duct. We suggest that congenital abnormalities of the cystic duct may be an important factor in a percentage of cases. Such abnormalities only become apparent if the duct is very carefully dissected and unless serial sections are made are easily overlooked. Unfortunately, only 3 of our 6 specimens were examined in detail, but in these three anatomical abnormalities were found. In one case the abnormality had been missed on routine pathological examination.

In *Case* 1 examination of the specimen showed a grossly enlarged gangrenous gall-bladder and 1·5 cm. of cystic duct. On serial section the distal end of the duct was found to be severely stenosed and divided into two narrow channels.

In *Case* 5 examination of the specimen showed the gall-bladder walls to be normal with a pigment stone lying in Hartmann's pouch (*Fig.* 197). On serial section the cystic duct was found to split into numerous narrow ducts lined by columnar or cuboidal epithelium.

In *Case* 6 the gall-bladder was chronically inflamed, with thickened walls and a whitish stone lying in Hartmann's pouch (*Fig.* 198). On careful dissection of the cystic duct, which was embedded in a mass of fibrous tissue, a second stone was found to lie in a narrow diverticulum opposite to Hartmann's pouch. The cystic duct was much dilated and ran around the diverticulum; at a point about 1·5 cm. away

from the gall-bladder there was a narrow stricture in the duct which failed to admit the finest probe. Distal to the stricture the duct was of normal calibre (*Fig.* 199).

A malformation of the cystic duct was therefore present in 2 cases of cholelithiasis and in the 1 case of gangrenous cholecystitis.

Gangrenous cholecystitis is rare, even in adults. Sobel (1938) states that Judd (1934) found only 0·7 per cent of gangrenous or perforated gall-bladders in 9446 operations on adults suffering from biliary diseases. Potter (1938) could find only 17 children with gangrenous or perforated gall-bladders in the literature, 15 of them being secondary to typhoid fever.

In conclusion, it is stressed that gall-bladder disease in childhood is not just a pathological curiosity, but is not too uncommon. It is reasonable to suppose that mild attacks of cholecystitis escape recognition and that cases could be found amongst the enormous number of children with undiagnosed abdominal pain that clutter up all pædiatric and surgical pædiatric out-patient departments. It is also reasonable to suggest, as did Graham (quoted by Montgomery, 1932) that many cases of cholecystitis first recognized in middle life had their inception in childhood.

SUMMARY

A not inconsiderable number of cases of gall-bladder disease in children is recorded in the literature. In the majority, no satisfactory explanation of the pathology is postulated. We suggest that congenital abnormality of the cystic duct is an important factor in many cases of cholecystitis in children.

REFERENCES

BONTA, J. A., and LOVINGOOD, C. G. (1952), *Surgery*, **31**, 309.
BOOKER, L. (1952), *J. Pediat.*, **40**, 667.
EDINGTON, C. H., (1930), *Brit. med. J.*, **1**, 782.
GAIRDNER, D., (1939), *Arch. Dis. Childh.*, **14**, 109.
GIBSON, J., (1734), *Medical Essays and Observations*, **2**, 353. Edinburgh.
GROSS, R. E. (1953), *The Surgery of Infancy and Childhood*, Philadelphia and London: Saunders.
JONES, R. N. (1951), *Lancet*, **1**, 324.
JUDD, E. S. (1934), *Minnesota Med.*, **17**, 576.
LOWENBURG, H., and MITCHELL, A. G. (1938), *J. Pediat.*, **12**, 203.
MONTGOMERY, A. H. (1932), *Amer. J. Dis. Child.*, **44**, 372.
POTTER, A. H. (1938), *Surg. Gynec. Obstet.*, **66**, 604.
REID, M. R., and MONTGOMERY, J. C. (1920), *Bull. Johns Hopk. Hosp.*, **31**, 7.
SCHOTTMUELLER, H. (1931), *Klin. Wschr.*, **10**, 17.
SOBEL, I. P. (1938), *Arch. Pediat.*, **55**, 669.
SWING, A. T., and BULLOWA, J. G. M. (1919), *Ann. Surg.*, **69**, 534.
SYNDER, W. H., CHAFFIN, L., and OETTINGER, L. (1952), *J. Amer. med. Ass.*, **149**, 1645.
ULIN, A. W., NOSAL, J. L., MARTIN, W. L. (1951), *J. Amer. med. Ass.*, **147**, 1443.
— — — — — — (1952), *Surgery*, **31**, 312.

THE COMPLICATIONS OF 'OSTEITIS PUBIS'

INCLUDING A REPORT OF A CASE OF SEQUESTRUM FORMATION GIVING RISE TO PERSISTENT PURULENT URETHRITIS

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THE main complications of 'osteitis pubis' from the patient's point of view are pain and prolonged disability. From the point of view of the student of surgery the main complications are a lack of understanding as to the exact cause of the condition, dissatisfaction with nomenclature—for definition is largely a reflection of interpretation—and, consequently, difficulties with regard to treatment.

INCIDENCE

The incidence of 'osteitis pubis', though small, is significant on account of the length of the period of disablement which it causes and the pain to which the victim is subjected. It occurred in 1·7 per cent of 352 cases studied by the present writer where operation had been carried out for bladder-neck obstruction.

NOMENCLATURE

Customary long usage tends to retain in our vocabulary of medical and surgical definitions certain terms which have already been, or may later be, proved to be inaccurate. 'Osteitis pubis' as a descriptive title for an uncommon though most distressing complication of operative procedures and trauma in the neighbourhood of the interpubic disk of fibrocartilage would appear to have been introduced by Rochet and Legueu (1923). These authors described a complication which followed suprapubic cystotomy and which they called 'l'ostéite pubienne'. The following year, Edwin Beer (1924), through his own interest and classical writings at that time, started an effort, which has since been maintained, to find out more about the condition which he then called "periostitis of the symphysis and descending rami of the pubis following suprapubic cystotomy".

Although Kretschmer and Sights (1930) first used the term 'osteitis pubis', they still bracketed it with 'periostitis' in the title of their article recording an unusual case following suprapubic prostatectomy. In addition to the more usual features of the condition, this case presented sinuses discharging pus from tracts leading down to each ischial tuberosity.

Lazarus (1936) crystallized the terminology of the disease into ' osteitis pubis ', and this has since been retained as a descriptive title. It will without doubt remain with us for ever despite its evident inaccuracy.

At the conclusion of a review of the condition, arising largely following the fashionable retropubic method of prostatectomy, Mortensen (1951) wisely states that at present " the lack of aetiological information necessitates caution in prevesical surgery ". Similarly, lack of aetiological information has inevitably led to a lack of caution in the choice of a descriptive title for this complication of prevesical surgery.

The nomenclature of a disease which is ill-understood may frequently be best founded upon clinical study alone. A study at the bedside of the patient afflicted with ' osteitis pubis ' will leave no doubt in the clinician's mind that pain is not only dominant but agonizing. In addition to the constant and severe pubic, perineal, and radiating pain which invariably travels down the inner side of the thighs in the distribution of the obturator nerves, it is accompanied by violently painful clonic contractions of the adductor muscles of both thighs when the patient attempts to move in bed. Similar clonic spasms may be precipitated by minimal external stimuli, such as jogging the bed.

Support for a diagnosis of ' osteitis pubis ' is given by the X-ray photographs of the pelvis, for the next most dominant feature is the osteoporosis seen in the bony component of the symphysial synchondrosis. Of great importance is the fact that the osteoporosis is always bilateral. It occurs on each side of the interpubic disk of fibrocartilage and usually to an equal extent on each side (Wheeler, 1941). Wheeler uses this observation to add weight to his argument against infection as an aetiological factor. He writes : " Moreover, it is inconceivable that an infection would jump over the cartilaginous symphysis extending to an equal distance bilaterally." Jean Cibert (1952), in an academically agile manner, figuratively jumps, not laterally from side to side across the interpubic disk of fibrocartilage, but backwards and forwards across it. Drawing a parallel between osteoporosis of the digital phalanges which occurs in pulp space infections of the fingers and ' osteitis pubis ', he concludes that ' osteitis pubis ' is due to the persistence close to the symphysis, generally behind but occasionally in front, of a septic process which is the result of too early closure of muscular wall and skin. The present writer believes that it might be wise to steer a course between the troublesome Scylla and Charybdis of osteoporosis of the pubic bone and pause awhile at the interpubic disk of fibrocartilage itself. A study of its development, its blood-supply, and its morbid histology in ' osteitis pubis ', together with a consideration of the well-recognized dangers to which its blood-supply and nutrition are liable in trauma to the symphysis and retropubic operations (Kirz, 1947), may reveal that the primary lesion is avascular necrosis of the interpubic disk of fibrocartilage and that the osteoporosis is a complication of this condition.

Brailsford (1953), in a discussion on osteochondritis and avascular necrosis, recalls John Hunter's explanation of the mechanisms and changes associated with avascular necrosis. Hunter states : " When a piece of bone becomes absolutely dead "—and why should not the word fibrocartilage be substituted—" it is then to the animal machine as any other extraneous body and adheres only by the attraction of cohesion to the machine. The first business of the machine therefore, is to get rid of the cohesion and discharge it. For effecting this separation there are several and successive natural operations going on. The first effect of the stimulus is on the surface of the living bone which becomes inflamed ; whether new vessels are formed or the old ones become enlarged is undetermined, but by injecting the surface of the part it eventually appears more vascular than the other parts. The surrounding parts are also inflamed, as the periosteum and cellular membrane, and often there is an ossific inflammation. This produces another process, first absorption of the earthy matter, and all the surface between the living bone and dead bone "—and why should not the words living bone and dead fibrocartilage be substituted—" become soft as if steeped in acid, while the dead parts remain as hard as ever. To complete the separation, the absorbents continue their office and absorb the living parts also."

In view of these two dominant features of the disease, pain and osteoporosis, the nomenclature used by Breton (1951), ' osteoporosa dolorosa of the pubis ' fits it admirably from clinical, radiological, and operative points of view.

SEQUESTRUM FORMATION

In the process of separation of dead from living bone in the human, the extrusion of dead pieces of inorganic matter—sequestra—is a common occurrence. The autolysis of soft tissues such as fibrocartilage results in no inorganic residue to be discharged from the body. If the hypothesis of avascular necrosis of the interpubic disk of fibrocartilage is correct, then it is not surprising that sequestrum formation is uncommon in ' osteitis pubis '.

Dinan (1939), in discussing two cases of pyogenic osteomyelitis of the pubic bone, considers that the great distinguishing feature between osteomyelitis of the pubis and ' osteitis pubis ' is the absence of sequestrum formation in the latter. Henderson (1950), though mentioning sequestrum formation in ' osteitis pubis ', considers that it only arises if a more virulent infection such as with *Staphylococcus aureus* is present. His conclusion as to the aetiology of the condition is that it is due to a low-grade cellulitis as a result of prostatic infection. This author points out other differences between osteomyelitis of the pubis and ' osteitis pubis '. In ' osteitis pubis ', repair is not associated with deformity of trabecular structure. In addition, osteomyelitis is a disease of children in whom the blood-supply of the pubic bone is different from that in the adult.

Abeshouse and Gellman (1943) state that sequestrum formation in ' osteitis pubis ' has not been reported, and Klinefelter (1950), in a review of the literature, also states that sequestrum formation does not occur. However, I believe that in the case recorded below the sequestrum arose directly as a result of ' osteitis pubis '.

CASE REPORT

A. P., aged 62, attended hospital on March 17, 1950, with symptoms of bladder-neck obstruction due to enlargement of the prostate.

Retropubic prostatectomy was performed on April 14. Section of the gland showed a simple adenomatous hyperplasia. Post-operatively he developed a mild right-sided epididymitis and was discharged from hospital thirty-six days after operation with a dry suprapubic wound and normal micturition.

FIG. 200.—Radiograph of the pubis symphysis, showing an abnormally wide gap between the pubic bones and the signs of 'osteitis pubis'.

Eight weeks after operation, symptoms and signs of 'osteitis pubis' appeared. Pain commenced in the perineum, radiated to the left knee down the inner side of the thigh, and was accompanied with localized tenderness over the symphysis pubis. There was no difficulty with micturition and the suprapubic wound remained dry.

With continued rest the pain largely disappeared, but the patient continued to complain of perineal pain, which was worse on sitting and on attempting to ride a bicycle.

A radiograph on Aug. 10 (*Fig.* 200) showed an abnormally wide gap between the pubic bones and suggested 'osteitis pubis'.

The condition appeared to resolve finally in December, 1950, i.e., eight months after the prostatectomy. Eleven months after this original operation, the patient attended the out-patient department complaining of dysuria of one month's duration. He was found to have a purulent urethritis and left-sided epididymitis due to *Staphylococcus pyogenes*. After initial response to antibiotics and chemotherapy the condition relapsed and at urethroscopy a stricture was seen at the membranous urethra. There was a great deal of surrounding granulation tissue. With further antibiotic treatment the purulent urethral discharge lessened and there was present only a little white glairy morning discharge. It was decided to commence urethral dilatations with gum-elastic bougies. This was followed by the occurrence of further epididymitis which subsequently subsided. At the resumption of urethral dilatation a grating sensation was noticed and a calculus suspected.

A further radiograph of the pelvis showed sclerosis of the pubic bones following healing of the 'osteitis pubis'. A shadow was noted in the P–A views which was thought could be in the posterior urethra and which had the appearances of a sequestrum (*Fig.* 201).

FIG. 201.—Radiograph of the pubic symphysis, showing sclerosis of the pubic bones following healing of the 'osteitis pubis' and a shadow corresponding to the sequestrum later removed from the urethra.

He was re-admitted to hospital on July 26, 1951, and at urethroscopy a mass of granulation tissue was seen at the junction of the bulbous and the membranous urethra. At this point there was noted the distal end of a spicule of bone which was removed with crocodile forceps. Immediate convalescence was uneventful and he was discharged home four days later with normal micturition. He had to be re-admitted to hospital however on Sept. 8 for incision of a left scrotal abscess. His final convalescence was satisfactory, and *Fig.* 202 shows the final X-ray appearances.

This case of sequestrum formation following 'osteitis pubis' is unusual. Moschowitz (1927) describes 2 cases which are, however, best excluded from any accurate review of recorded cases of 'osteitis pubis'. The first case was that of a female machinist who accidentally sat on an oil-can. Osteomyelitis of the pubis arose, followed by sequestration of the pubic bone. In the second patient a prostatic abscess was followed by a pelvic abscess, osteomyelitis of the left pubis, and sequestrum formation. Jentzer (1934) described the case of a female, who, two weeks following symphysiotomy for difficult labour, developed pubic pain and a discharge from the wound. Pain was present on walking and the patient's gait resembled that associated with bilateral congenital dislocation of the

hips. Five months after delivery, radiography revealed a 20-mm. separation of the symphysis, destruction of bone, rough edges, and small sequestra. The observations suggest that this case may have been one of 'osteitis pubis'. Soderlund (1930) also described a case in which, after uncomplicated labour, pain in the perineum which radiated

FIG. 202.—Final radiographic appearances after removal of the urethral sequestrum.

down the lower extremities increased progressively for eighteen months. A vaginal discharge became manifest and was traced to a sinus communicating with the pubic bone. A sequestrum was removed and cure resulted. Fischer (1949) records 2 cases of 'osteitis pubis', one occurring one month after Freyer's prostatectomy where the operation was difficult and periosteal injury seemed likely. In the second case the condition arose two months after a retropubic prostatectomy. In both cases an abscess formed and, later, sequestra were evacuated. These authors conclude that there are two precipitating factors in 'osteitis pubis': first, injury to the bone or periosteum; and, secondly, infection of the wound—usually by urine containing staphylococci, *B. coli*, or Proteus organisms.

URINARY AND OSSEO-URINARY FISTULA

Pierson (1929) described the formation of a urinary fistula as a result of 'osteitis pubis'. This author reported 4 cases of 'osteochondritis of the symphysis pubis'. One case followed bilateral inguinal herniorraphy. An infected sinus healed only after five years. Two and a half years later a swelling appeared at the site of the old sinus and this broke down to discharge pus and urine. Pierson concluded that the urinary fistula may have developed as a result of a prevesical abscess coming from the osteochondritis of the pubis. The abscess then ruptured into the urethra.

Abeshouse and Gellman (1943) report 24 cases of osseo-urinary fistula as a complication of injury and disease of the pelvic bones and head of the femur. There are references to seven cases in which, following osteomyelitis, the urethra was involved and sequestra were either passed or removed. I can find no previous record of a sequestrum arising as a result of 'osteitis pubis' making its way into, and having to be removed from, the urethra.

Nagel (1869) removed successfully by external urethrotomy several fragments of bone from the urethra of a young man aged 26 years who was suffering from frequency and painful micturition. The right hip-joint, which was ankylosed, had been the site of osteomyelitis in childhood.

Ungerer (1881), in a thesis, reported the case of a man aged 28 years who had a primary osteomyelitic lesion in both legs at the age of 14 years. At the age of 23 years the left hip was infected. The patient developed a left inguinal abscess accompanied by frequency and urgency of micturition due to fragments of bone in the urethra. An inguinal fistula draining pus and urine developed. After the spontaneous passage of a piece of bone the size of a kidney bean, further sequestra were removed by external urethrotomy.

Heydenreich (1892) reported the case of a female aged 40 years who had had osteomyelitis of the hip and the left pubic bone at the age of 6 years. Symptoms indicative of urinary lithiasis arose 28 years later and fragments of urinary calculi were passed through the urethra spontaneously. The removal of fragments of bone from the urethra by external urethrotomy completely relieved the patient's symptoms.

Sir Henry Thompson (1895) recorded the case of a female aged 40 years who had suffered from osteomyelitis of the right hip at the age of 17 years. Three abscesses arose around the hip-joint and after fifteen years symptoms of urinary lithiasis became manifest. A piece of bone, encrusted with phosphates, was removed from the bladder. There were two subsequent lithotomies and later a piece of bone was removed from the urethra with forceps.

Marenescu (1924) described a case in a female aged 39 years who developed frequency of micturition and hæmaturia as a result of osteomyelitis of the pubis. Cystoscopy revealed polyps in the bladder and mucosal plaques covered with urinary salts. This examination was followed eight days later by the passage of a sequestrum into the urethra. The sequestrum was removed with forceps and complete recovery resulted.

The importance of urethroscopy in the diagnosis of non-gonococcal urethritis is stressed by Glingar (1927) in describing a case of a male with urethritis, peri-urethritis, and bilateral inguinal adenitis. Urethroscopy revealed a bony sequestrum just proximal to the fossa navicularis. Cystoscopy revealed a scar on the bladder wall and X-ray examination showed an old lesion of osteomyelitis affecting the sacro-iliac joint. The significance of foreign bodies in cases of persistent urethritis is mentioned by Harkness (1950). Commonly, the

foreign body descends to the urethra from the upper urinary tract or is inserted by way of the external urinary meatus. Calculus foreign bodies may form behind a stricture, but this is not common.

usually associate with ' osteitis pubis '. Silver (1941), in recording 4 cases of ' osteitis pubis ' following suprapubic prostatectomy, describes one case in which the disease was complicated by involvement

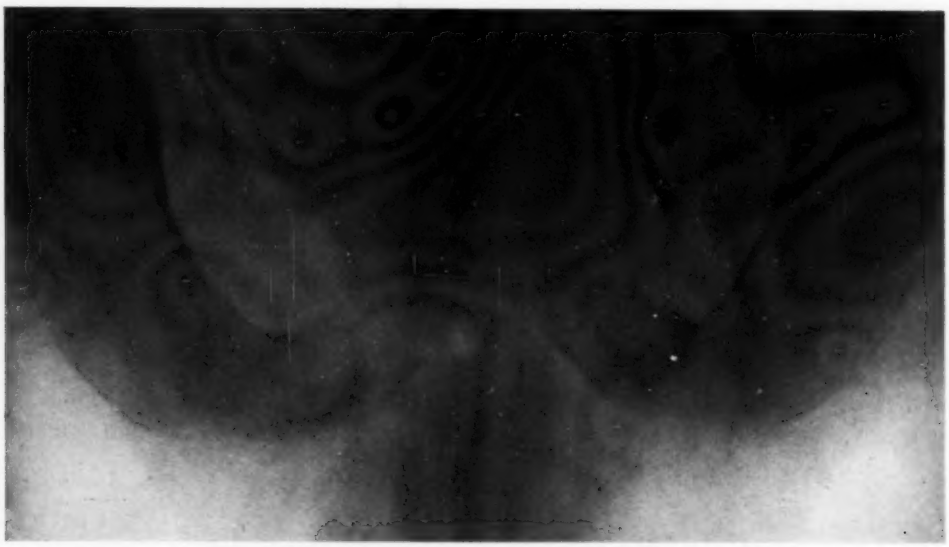

FIG. 203.—Radiograph of an early case of ' osteitis pubis ' showing osteoporosis of the ischial tuberosities.

FIG. 204.—Radiograph of a case of ' osteitis pubis ', showing more advanced osteoporosis in the ischial tuberosities as well as in the pubic symphysial area.

HETEROTOPIC BONE FORMATION

Before discussing the origin of a bony spicule such as was removed from the urethra in the case of ' osteitis pubis ' described above, it is wise to consider the phenomenon of heterotopic bone formation.

The feature of osteoporosis in ' osteitis pubis ' need not be confined to the body of the pubic bone. A frequent finding is porosis of the ischial tuberosities, and this is associated with severe localized pain and tenderness at these sites (*Figs.* 203, 204).

Rarely, the hip-joint may be involved by the same pathological process as that which we more

of the hip-joint. Similar appearances as were noted in the pubic bone were also seen in radiographs of the acetabulum and head of the femur. Friedenberg (1950) described a similar case.

A further complication of ' osteitis pubis ' associated with and adjacent to the areas of porosis in bone, is the formation of small spicules of bone. These spicules are noted on occasion outside the normal confines of the bony parts of the region. Such a phenomenon is seen most clearly in those cases where porosis has involved the ischial tuberosities (*Figs.* 205, 206).

At these sites bony formation appears to occur in the region of the attachment of muscles to the ischial tuberosities.

What is the origin of these spicules of bone? It is possible that they arise as the result of pyogenic osteomyelitis superimposed upon the original condition. Alternatively, they arise as a complication of the osteoporosis which occurs during the natural responses of bone adjacent to a dead structure, i.e., assuming avascular necrosis of the fibrocartilaginous disk to be the definitive morbid anatomical feature. In this case it may be heterotopic. Sudeck (1919) mentions the occasional case of heterotopic bone formation associated with 'osteitis' of the pubic bone occurring after operation.

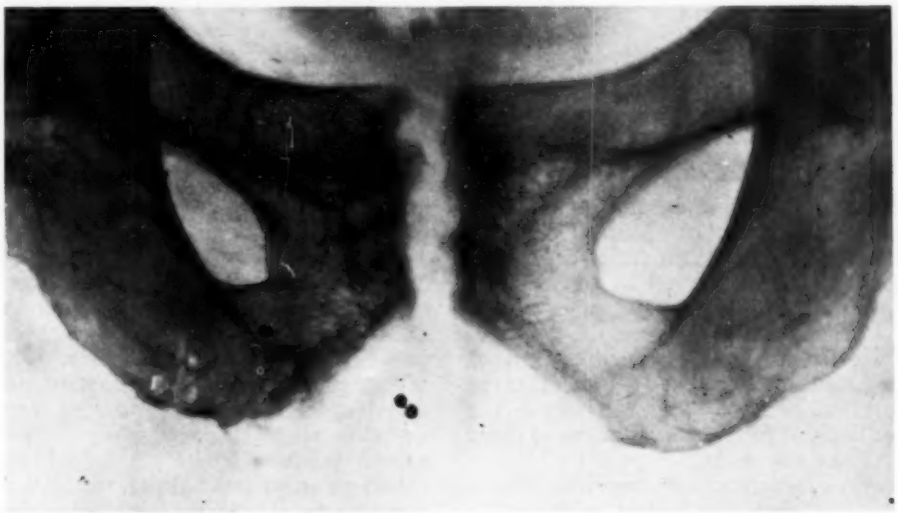

FIG. 205.—Radiograph of a case of 'osteitis pubis', showing new-bone formation in the region of the ischial tuberosity.

It is suggested that it may be profitable to consider whether there are not conditions pertaining in 'osteitis pubis' favourable to the production of heterotopic bone.

Sir Arthur Keith (1927) explains the production of heterotopic bone embryologically. However, following the observation of Bernasconi (1911), when for the first time a case was reported of heterotopic bone formation following suprapubic cystotomy, there have been 16 such cases described. Abeshouse (1948) added a further case and reviewed the condition. His conclusions are that new bone is found in three different parts of the wound—in the scar, in deep fascial tissues of the rectus muscle sheath, and in new connective tissue or granulation tissue. In some cases the new bone is attached to the pubic bone. Leriche and Policard (1928) consider that bone will form where there is an excess of calcium salts and an abundant blood-supply. It may be worthy of note here that urine in itself provides an abundance of calcium salts.

In addition, the epithelium of the urinary tract has unusual osteogenic properties. Strauss (1914) first demonstrated experimentally these properties. Repairing ureteric defects in dogs by means of pedicled abdominal-wall flaps, he found that a layer of bone developed in the portion of the flap bordering on the ureter. Neuhof (1917) described experiments in which bladder defects were repaired with fascia lata. He observed ossification on the border adjacent to the bladder lumen. Phemister (1923) repeated these experiments in dogs with the same results. However, in sheep, which are herbivorous animals with an alkaline urine, no ossification occurred.

All these facts would appear to support the theory of Abbott and Goodwin (1932) that histology rather than embryology is the factor to be considered in heterotopic bone formation. Huggins (1930) had previously put forward even more definite views that the factors essential to the production of heterotopic bone are, first, an epithelium with osteogenic stimulating power, and, secondly, a special type of connective tissue cell, i.e., ossifying fibroblasts. Urine was not considered to be a factor in the production of bone when fascial transplant to the bladder takes place. Huggins carried out experiments where the

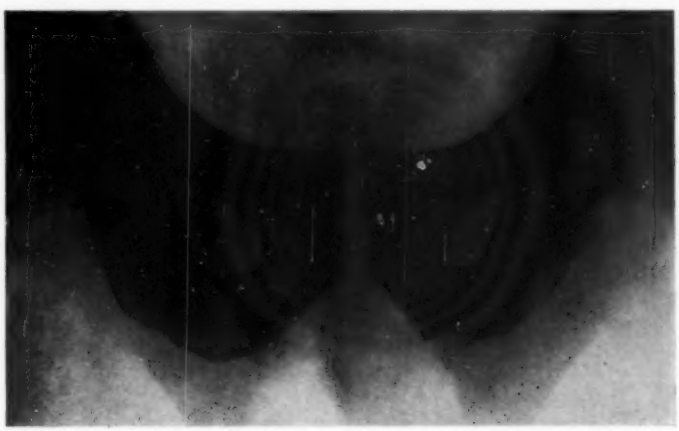

FIG. 206.—Radiograph of a case of osteitis pubis', showing new-bone flakes in the region of the osteoporotic ischial tuberosities.

urine was diverted from the bladder by transplanting the ureters to the groin. True spongy bone occurred around bladder, ureteric or renal pelvic mucosa when either was transplanted into the rectus muscle sheath, fascia lata, subcutaneous tissues, certain muscles, and synovial membrane. Transplants of renal parenchyma—cortex or medulla—prostatic tissue, gastric, jejunal, colonic, or gall-bladder mucosa, adrenal cortex, dura mater, and bone shavings implanted into the rectus muscle-sheath all failed to produce bone. Bladder, ureteric or renal pelvis transplanted into kidney, spleen, and liver, also failed to produce any ossification. Bone formation when it occurred took about sixty days.

The factor of an adequate blood-supply in the production of heterotopic bone is further amplified by the observation of Roome and McMaster (1934) that heterotopic bone formation following transplantation of vesical mucosa into muscles of a dog's leg was increased by venous stasis in the affected leg. Of some interest also in this present study is the report by Collins and Wheeler (1941) of an osteoma occurring in the bladder of a 67-year-old negress following radium and deep X-ray therapy for carcinoma of the cervix. They attributed the osteoma to thrombosis of blood-vessels of the bladder caused by radium and the deep X rays.

That biochemical factors are of some importance in the production of heterotopic bone is shown by the observations of Huggins (1931) and Dragstedt and Kearn (1932). The former observed that the phosphatase activity was higher in various stages of heterotopic bone formation occurring in vesical mucosa transplants. The latter two writers described experiments in which they slowed down the process of heterotopic ossification by parathyroidectomy which induced hypocalcæmia.

At present the origin of spicules and flakes of bone seen in radiographs of cases of ' osteitis pubis ' is conjectural. It may be stated, however, that on occasion the sequence of events may lead to pyogenic osteomyelitis with the production of sequestra. In addition, hyperæmia, an excess of calcium salts resulting from the decalcification of bone and the possible presence of urine, venous stasis resulting from either thrombosis of, or damage to, vessels, and the association of the condition with operations carried out on the urinary system whose epithelium has a peculiar osteogenic power, make it wise, I believe, not to dismiss the possibility of a heterotopic origin for these spicules and flakes of bone.

TREATMENT

The treatment of ' osteitis pubis ' is complicated by diversity of method. At present the methods of treatment are multifarious and are all alike in being unsuccessful in markedly lessening the prolonged period of disability. Rest in bed, local rest of the pelvic girdle by the application of a plaster-of-Paris hip spica, the administration of analgesics, and considerable patience are the mainstays of treatment at present.

Vitamin B_1 (Lavalle and Hamm, 1949), short-wave diathermy and deep X-ray therapy (Goldstein and Rubin, 1947; Lavalle and Hamm, 1949; Leucutia, 1951) are popular ancillary methods of treatment. Recently, some success has been claimed for cortisone in the treatment of ' osteitis pubis ' (Woodall, 1952; Marshall and others, 1952). Obturator neurectomy is advocated by Lowsley and Gentile (1948) and Muschat and others (1952). This operation would appear to be both justifiable and valuable in those cases where very intense and painful adductor muscle spasms occur. Of historical interest are such methods of treatment as spinal chordotomy (Cohen, 1946), excision of the area of pubic bone affected (Pierson, 1929; Silver, 1941) and wiring of the symphysis pubis (Lazarus, 1936). More recently Adams and Chandler (1953) recorded a case of ' osteitis pubis ' treated by resection of the symphysis and bridging of the defect by an autogenous tibial bone-graft. These authors' contribution is of great value for three reasons: First, by drawing attention to external trauma to the symphysis pubis as an occasional cause of ' osteitis pubis '; secondly, valuable histological studies of the excised tissues are presented; and thirdly, as a result of the graft having to be removed later, an illustration is given of the fact that the symphysis pubis can be completely excised without adversely affecting the patient's locomotion or giving rise to any symptoms.

DISCUSSION

What may be termed the ' complications ' of ' osteitis pubis ' have been presented for discussion in the light of the hypothesis of avascular necrosis of the interpubic disk of fibrocartilage as the cause of the condition.

Entering the structure from the posterior aspect, and clearly seen at retropubic operations, are vessels arising from the pubic branches of the obturator and inferior epigastric arteries. Francis (1952) mentions, in addition, branches of the internal pudendal and medial femoral circumflex arteries as supplying the tissues of the symphysial synchondrosis. Entering the anterior aspect of the joint are the pubic branches of the superficial external pudendal artery. The vessels entering the posterior aspect may suffer injury during retropubic operations as a result of direct trauma, e.g., in the use of the ' boomerang ' needle, careless application of ligatures, excessive use of the diathermy coagulating current. After operation, phlebothrombosis or septic thrombophlebitis may be the responsible factor. The vessels entering the anterior aspect of the synchondrosis are unlikely to be damaged except in those cases which arise as a result of external trauma.

Kirz (1947) lays admirable emphasis upon measures which should be taken during retropubic operations in order to avoid injury to the posterior aspect of the symphysis pubis and describes a procedure especially designed to avoid such injury.

The cases described by Klinefelter (1950) and Adams and Chandler (1953) would appear to be true cases of ' osteitis pubis ' due to external trauma. Pierson (1929), Painter (1930), and Burman and others (1934), each described a case which Adams and Chandler quote as additional cases of ' osteitis pubis ' due to external trauma. It is doubtful, however, whether these three cases should be included in an accurate collection of cases of ' osteitis pubis '.

The two cases described by Söderlund and Jentzer illustrate, I believe, the resulting damage to the nutrition of the symphysial joint from labour and symphysiotomy.

In Adams and Chandler's paper, the naked-eye and histological appearances of the excised symphysial tissues is described. They write: "The lesion appeared yellow in colour, was firm and gritty in consistency, and contained irregularly arranged bony spicules." The present writer hopes in a subsequent communication to comment on the results of surgical excision of the interpubic disk of fibrocartilage in cases of 'osteitis pubis'. The yellow colour of the disk at such operations is striking, and to the naked-eye at once suggests death of this tissue. Adams and Chandler report the occurrence of degeneration of the hyaline cartilage present in the disk, evidence of active bone resorption, fibrous tissue replacement, and the cellular picture of a low-grade inflammation.

The explanation for the involvement of the hip-joint in some few cases of 'osteitis pubis' is bound to be highly conjectural. Maximow and Bloom (1952) note the presence of fibrocartilage in the ligamentum teres of the femur. The posterior terminal branch of the obturator artery provides an acetabular branch, which, passing through the acetabular notch, supplies the ligamentum teres and the head of the femur. Damage to this vessel or its involvement in pelvic thrombosis due to a low-grade cellulitis, though less likely, is surely as possible as similar damage to the vessels supplying the interpubic disk of fibrocartilage.

If the hypothesis of avascular necrosis of the interpubic disk of fibrocartilage could be proved, there would, I believe, be a collation and explanation of all those complex features of the condition which we call 'osteitis pubis'. The painful osteoporosis would, under these circumstances, be an expression of the natural phenomena which John Hunter described. Pelvic venous thrombosis, increased vascularity, the abundance of calcium salts in the areas surrounding the osteoporotic parts, together with the possible escape of urine from any imperfectly closed surgical incision, make conditions which could be considered suitable for the formation of heterotopic bone. Secondary infection as well as providing a stepping stone towards the extrusion of sequestra and the formation of urinary and osseo-urinary fistula, might well also be responsible for the occurrence of a true pyogenic osteomyelitis in addition to the 'osteitis pubis'.

Such a hypothesis might in addition make treatment—at present complicated—the simple and safe operative procedure of excision of the dead interpubic disk. This procedure might be found to avoid all the complications associated with the natural responses to the presence of this dead tissue and to reduce very considerably the duration of the disablement.

Lastly, this hypothesis, if proved correct, would transform the complication of inaccurate nomenclature into scientific terminology and 'osteoporosis dolorosa of the pubis' would be recognized as avascular necrosis of the interpubic disk of fibrocartilage due to operative procedures and trauma in the neighbourhood.

SUMMARY

1. The incidence and the history of nomenclature of 'osteitis pubis' are discussed.

2. The complications associated with the condition are enumerated and discussed.

3. A case of sequestrum formation giving rise to persistent purulent urethritis is reported.

4. The complications, treatment, and nomenclature of 'osteitis pubis' are considered in the light of the hypothesis of avascular necrosis of the interpubic disk of fibrocartilage as the aetiological factor.

For permission to publish the case here recorded I am indebted to Mr. H. O. Blauvelt, Chase Farm Hospital, Enfield, at which hospital I was given the opportunity to study and treat this and other cases of 'osteitis pubis'.

I am also grateful for the opportunity afforded me to study the series of cases of bladder-neck obstruction mentioned in the text and which were operated upon by Mr. H. O. Blauvelt, Mr. T. Max Pemberton, and other surgical colleagues.

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REFERENCES

ABBOTT, A. C., and GOODWIN, A. M. (1932), *Canad. med. Ass. J.*, **26**, 393.
ADAMS, R. J., and CHANDLER, F. A. (1953), *J. Bone Jt Surg.*, **35A**, 685.
ABESHOUSE, B. S. (1948), *J. Urol.*, **59**, 50.
— — and GELLMAN, M. (1943), *Urol. cutan. Rev.*, **47**, 88.
BEER, E. (1924), *Int. J. Med.*, **37**, 224.
BERNASCONI (1911), *Ass. franç. Urol.*, (Proc: Verb:) **15**, 746.
BRAILSFORD, F. J. (1953), *The Radiology of Bones and Joints*, 5th ed., 716. London: Churchill.
BRETON, P. M. (1951), *Arch. esp. Urol.*, **7**, 227.
BURMAN, M., WEINKLE, I. N., and LANGSAM, M. J. (1934), *J. Bone Jt Surg.*, **32**, 649.
CIBERT, J. (1952), *Brit. J. Urol.*, **24**, 213.
COHEN, J. (1946), *J. Urol.*, **55**, 84.
COLLINS, C. W., and WHEELER, F. J. (1941), *Ibid.*, **46**, 494.
DINAN, J. J. (1939), *Canad. med. Ass. J.*, **41**, 436.
DRAGSTEDT, G. A., and KEARN J., E., jun. (1932), *Amer. J. Physiol.*, **100**, 262.
FISCHER, F. (1949), *Nord. Med.*, **41**, 61.
FRANCIS, C. C. (1952), *The Human Pelvis*, 46. St. Louis: C. V. Mosby Co.
FRIEDENBERG, Z. B. (1950), *J. Bone Jt Surg.*, **32A**, 924.
GLINGAR, A. (1927), *Wien. klin. Wschr.*, **40**, 166.
GOLDSTEIN, A. E., and RUBIN, S. W. (1947), *Amer. J. Surg.*, **74**, 480.
HARKNESS, A. H. (1950), *Non-gonococcal Urethritis*, 158. Edinburgh: Livingstone.
HENDERSON, D. StC. L. (1950), *Brit. J. Urol.*, **22**, 30.
HEYDENREICH, A. (1892), *Rev. méd. Est.*, **24**, 6.
HUGGINS, C. B. (1930), *Proc. Soc. exp. Biol., N.Y.*, **27**, 753.
— — (1931), *Biochem. J.*, **25**, 728.
JENTZER, A. (d.) (1934), *Rev. Orthoped.*, **21**, 289.
KEITH, Sir A. (1927), *Proc. R. Soc. Med.*, **21**, 301.
KIRZ, E. (1947), *Brit. J. Surg.*, **34**, 272.
KLINEFELTER, E. W. (1950), *Amer. J. Roentgenol.*, **63**, 368.
KRETSCHMER, H. L., and SIGHTS, W. P. (1930), *J. Urol.*, **23**, 573.
LAVALLE, L. L., and HAMM, F. C. (1949), *Ibid.*, **61**, 83.
LAZARUS, J. A. (1936), *Ann. Surg.*, **103**, 310.

LERICHE, R., and POLICARD, A. (1928), *Normal and Pathological Physiology of Bone.* London: Henry Kimpton.
LEUCUTIA, T. (1951), *Amer. J. Roentgenol.*, **66**, 385.
LOWSLEY, O. S., and GENTILE, A. (1948), *J. Urol.*, **59**, 281.
MARENESCU, G. (1924), *J. Urol. méd. chir.*, **18**, 470.
MARSHALL, V. F., WHITMORE, W. F., jun., PETRO, A. J., POPPELL, J. W., GRANT, R. N., and RAWSON, R. W. (1952), *J. Urol.*, **67**, 364.
MAXIMOW, A. A., and BLOOM, W. (1952), *A Textbook of Histology*, 10th ed., 616. Philadelphia: W. B. Saunders Co.
MORTENSEN, H. (1951), *J. Urol.*, **66**, 412.
MOSCHOWITZ, A. V. (1927), *Ann. Surg.*, **85**, 792.
MUSCHAT, M., LEVENTHAL, G. S., and KRAUSE, J. (1952), *J. Urol.*, **68**, 552.
NAGEL, A. (1869), *Allg. wien. med. Ztg.*, **14**, 122.
NEUHOF, H. (1917), *Surg. Gynec. Obstet.*, **49**, 834.
PAINTER, C. F. (1930), *New Engl. J. Med.*, **202**, 585.
PEIRSON, E. L. (1929), *Surg. Gynec. Obstet.*, **49**, 834.
PHEMISTER, D. B. (1923), quoted by MCWORTER, G. L. (1929), *Surg. Gynec. Obstet.*, **49**, **205**.
ROCHET, X. and LEGUEU, X. (1923), *J. Urol. méd. chir.*, **15**, 1.
ROOME, N. W., and MCMASTER, P. E. (1934), *Arch. Surg., Chicago*, **29**, 54.
SILVER, C. M. (1941), *Bull. Hosp. Jt Dis.*, **2**, 10.
SÖDERLUND, G. (1930), *Acta chir. scand.*, **67**, 850.
STRAUSS, A. A. (1914), *Surg. Gynec. Obstet.*, **17**, 78.
SUDECK, P. (1919), *Dtsch. Z. Chir.*, 105.
THOMPSON, Sir H. (1895), *Clinical Lectures on Diseases of the Urinary Organs*, 4th ed., 288.
UNGERER, L. (1881), *Thés. de Strasbourg.*
WHEELER, K. W. (1941), *J. Urol.*, **45**, 467.
WOODALL, W. M. (1952), *J. med. Ass. Albama*, **21**, 258.

PHÆOCHROMOCYTOMA

A REPORT OF TWO CASES WITH A REVIEW OF THE DIAGNOSTIC TESTS

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WHILST the pathogenesis of essential hypertension is uncertain and its treatment empirical, the clinical and laboratory investigation to which these patients are now subjected sometimes reveals an unsuspected cause for the elevated blood-pressure which is amenable to surgical treatment, such as unilateral renal disease and endocrine disorders.

Amongst the latter are the adrenaline-producing tumours of the adrenal medulla known as phæochromocytomas. The first account of the clinical manifestations of a phæochromocytoma was published only thirty years ago by Labbé (Labbé, Tinel, and Doumer, 1922) the first operative success being recorded by Pincoffs in 1929. Proof of the humoral cause of the hypertension came from Beer, King, and Prinzmetal, who in 1937 showed that there was a pressor substance in the plasma at the time of a paroxysm. Recent advances have enabled the diagnosis to be made more frequently, and Smithwick (1951) found 6 patients with tumours in his series of 1200 undergoing sympathectomy for hypertension.

CASE REPORTS

Case 1.—This man, aged 48 years, came to the eye clinic because of transient blurring of the vision accompanied by slight defects in both temporal fields lasting at the longest for a few hours. The retinal appearance was that of early hypertension and his urine was found to have a trace of albumin. He later added to his history headache, palpitations accompanied by sweating and prostration, and tightness in the chest, making light of his visual upsets. His urine contained a trace of albumin and a little sugar and his blood-pressure was 160/90.

Because of these findings and the 'spastic' appearance of the retinal arterioles he was admitted, as these so-called 'vascular spasms' causing transient field defects or weakness of a limb sometimes herald a more serious accident. When in the ward he said that these 'turns' of headache, thumping heart, sweating, and restlessness were all of the same nature, though varying in duration and severity and had first troubled him as long ago as 1945, in retrospect being wrongly attributed to malaria relapses. His blood-pressure had been normal in 1939 and whilst he was in the army during the war, but by 1947 it was sufficiently high for an insurance company to load his premium. From an occasional attack with many months of freedom his symptoms had steadily progressed until in 1951 he had these unpleasant turns several times a week and was treated for 'hyperhydrosis' because of the drenching nocturnal sweats.

Whereas the resting B.P. lay between 130/90 and 160/100 it was elevated to 210/110 or 280/150 at times and there could be no doubt about the diagnosis of paroxysmal hypertension probably due to a phæochromocytoma. Most often a paroxysm would start as he was about to go sleep; the sweating started behind the ears and spread to his head and trunk, he became pale, his heart thumped slowly and regularly, the headache developed gradually, his hands were tremulous, and he became very apprehensive and restless. After one and a half to two hours these symptoms and signs would slowly subside, his blood-pressure would fall, though still above the resting level, and he would fall asleep.

Because of his aggressive manner and wartime experiences he had extensive psychiatric examinations without much effect, and the possibility of acute anxiety was considered.

ON EXAMINATION.—A heavy built plethoric man of the hypertensive type. Physical examination between attacks revealed nothing of note and the retinal changes were minimal. Because of obesity a small abdominal mass was unlikely to be felt. B.P. 130/90 to 160/100 between attacks.

Investigations.—

Urine: Occasional trace of sugar and albumin plus a few R.B.C.'s

Renal function tests and I.V.P.: Normal.

Chest radiography: A normal cardiac contour.

E.C.G.: Flattened T waves in V5 and V6 suggesting ischæmia of the left ventricle.

Glucose tolerance test: Fasting 104 mg., rising to 228 mg. at one hour, returning to normal by two hours, with slight glycosuria.

Special Tests for Phæochromocytoma:—

Intravenous histamine: A slight rise from 175/108 to 202/130 six minutes after 0·025 mg. A second test with 0·05 mg. was negative.

Piperoxane test: During a paroxysm 20 mg. I.V. lowered the B.P. from 260/130 to 170/90 in three minutes, returning to 240/120.

Regitine test: After 7 mg. I.V. there was a rapid fall from 250/138 to 168/90, rising slowly to 200/105.

possibility of a local vascular tumour was considered, but neurological investigation was not helpful and attention was turned to her hypertension. She did not give a history so typical of paroxysmal hypertension as the first patient. She did not sweat or shake, but went pale at the

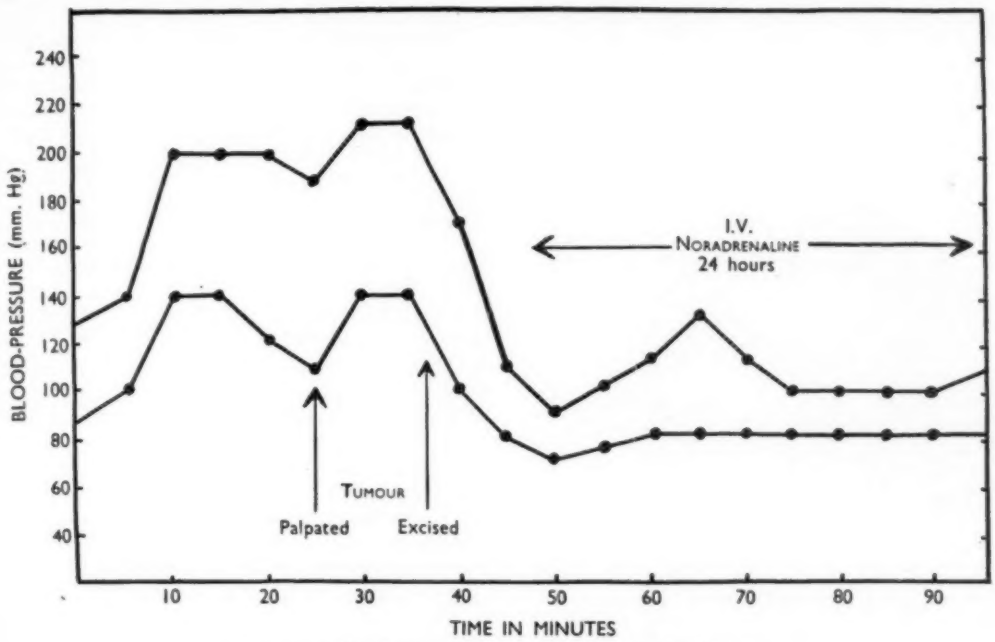

FIG. 207.—Blood-pressure during and after operation (*Case* 1).

AT OPERATION (A. J. H.).—A preliminary laparotomy revealed a tumour in the right suprarenal the size of a flattened golf ball. Some two weeks later this was removed through an incision in the loin and was found to be a typical phæochromocytoma 3·5 by 4·5 g. in size, well encapsulated with many blood-vessels in its rather friable substance. During the induction of anæsthesia his blood-pressure rose immediately on both occasions to above 200/140 and remained so until the tumour had been excised. (*Fig.* 207.) Within five minutes it had dropped to 90/70. Intravenous noradrenaline was given at once in normal saline at a rate varying from 8 to 32 a minute in order to keep the pressure about 130/70 and had to be continued for 24 hours before a reasonable level was maintained spontaneously.

PATHOLOGICAL SPECIMEN (*Fig.* 208).—This weighed 28 g. and histologically was composed of large cells containing neutral fat and anisotropic lipoids which gave positive tests with chromaffin and adrenaline stains. Biological assay of the tissue showed that it contained 1·6 mg. of *l*-noradrenaline and 0·1 mg. of *l*-adrenaline per gramme of substance wet weight. There was no evidence of malignancy.

POST-OPERATIVE PROGRESS.—He recovered slowly from the last operation, but in the past eighteen months he has been essentially well and his blood-pressure remains at 130–140/90. He has had no more attacks.

Case 2.—This woman of 48 years attended the neurological clinic because of recurrent headaches. Since a child of 8 she had been troubled by migraine, the headache being generalized, preceded by visual upsets, and accompanied by nausea and vomiting. Both her parents had similar trouble and the diagnosis did not seem to be in doubt.

Two years before coming to hospital, however, she noticed a new symptom, a transient fullness and throbbing in the left temporal region which would last about half an hour and might recur several times in a day. The time of the temporal discomfort. These episodes lasted about half an hour, when she appeared pale, restless, and anxious but never perspired; her pulse was of high

FIG. 208.—Cut surface of tumour from *Case* 1, showing large blood-vessels in its substance, with adrenal cortex attached inferiorly. (Approximate size, 4·5 × 3·5 cm.)

tension, rate about 80. She preferred to sit up in bed because of shortness of breath and retrosternal tightness of a mild degree.

Her blood-pressure varied at rest from 190/130 to 220/130, and in an attack was found to be 250/160, the highest blood-pressure recorded being 300/190.

ON EXAMINATION.—A rather thin spinster. The peripheral arteries were thickened, the left ventricle enlarged with apex beat in the fifth space 4½ in. from the midline; during an attack the first mitral and second aortic sounds became accentuated though the heart-rate did not increase.

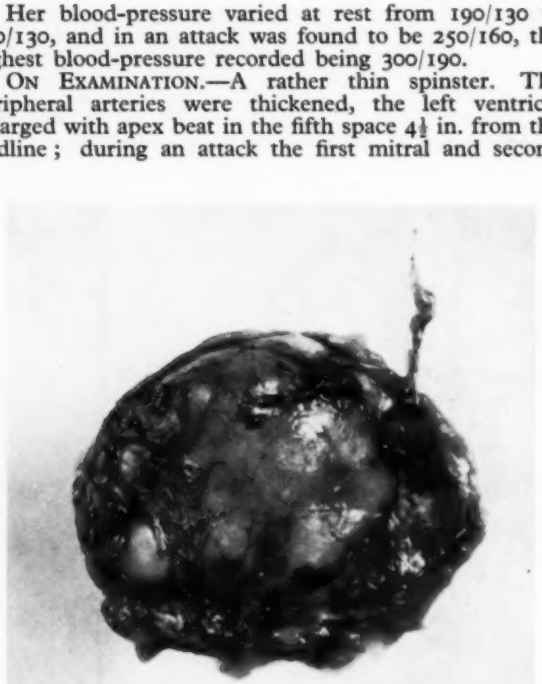

FIG. 209.—External appearance of tumour from *Case* 2 (approximate size, 3·0 × 3·2 cm.).

The optic fundi were within normal limits, but after operation a small patch of soft exudate appeared in the left eye which cleared after six weeks.

Investigations.—

Urine: Normal.

Renal function: Normal.

I.V.P.: No indication of a tumour.

Fasting blood-sugar: 230 mg./100 ml.

Chest radiography: Slight left ventricular hypertrophy.

E.C.G.: The T waves were a little flat in V4, 5, and 6, increasing in voltage after operation.

Special Tests for Phæochromocytoma:—

Intravenous histamine test: Not done owing to sustained hypertension.

Piperoxane test: After 11 mg. I.V. the B.P. fell from 160/115 to 130/90 in two minutes, rising to the original level rapidly.

Regitine test: B.P. fell from 190/120 to 154/90 within ten minutes of giving 5 mg. intramuscularly. During a paroxysm it fell from 300/190 to 130/80 and the symptoms were soon relieved.

Urinary pressor amines (biological assay): 599 mg. noradrenaline and 3 μg. adrenaline per litre and 780 μg. and 24 μg. respectively on a second occasion. (Normal total pressor amines about 50 μg.)

AT OPERATION (A. J. H.).—Having proved beyond doubt that an adrenaline-producing tumour was present, localization was necessary and a preliminary laparatomy was carried out.

A somewhat flattened roundish tumour 3 cm. in diameter was palpated in the right adrenal. Her blood-pressure rose sharply to 300/190, but had fallen to 220/142 by the time the midline incision had been closed and an approach made in the loin. Once it had been removed, in fragments owing to its friability, there was the anticipated drastic fall of blood-pressure to 90/60 and large amounts of noradrenaline in saline up to 100 μg. a minute were necessary to achieve a satisfactory level. After 30 hours the drip was discontinued with safety, though she too was very exhausted by the operation.

PATHOLOGICAL SPECIMEN (*Fig.* 209).—Owing to its vascularity and fragmentation the weight could not be determined, but it was similar in shape and appearance to the other tumour. Histologically there were the same polygonal cells with many vascular channels and no sign of malignancy. The chromaffin stains were misleading but the adrenaline stains were positive.

A pressor amine assay revealed 9·8 mg. *l*-noradrenaline and 1·7 mg. *l*-adrenaline per gramme of tissue.

POST-OPERATIVE PROGRESS.—Though she has had no more temporal headaches her blood-pressure has risen from the immediate post-operative level of 140/85 to about 170/90.

CLINICAL FEATURES

These two patients exhibited most of the features associated with adrenaline-producing tumours which, so far as the hypertension is concerned, may present with true paroxysmal hypertension, as in the first case, or as a sustained hypertension elevated at times to peak levels. It is this latter type, exemplified by the second patient, which presents the greatest diagnostic difficulty since the exacerbation of symptoms may be passed off as 'spasm' or a hypertensive crisis. In such cases of sustained hypertension any degree of essential hypertension may be mimicked and a proportion of patients present with papill-œdema and malignant hypertension, left ventricular failure, or cerebral hæmorrhage. There can be no doubt that close observation of the attack is of the greatest diagnostic help.

The pallor, restlessness, and tremor produced by a rapid liberation of adrenaline contrasts clearly with the plethora of the essential hypertensive. Because of the excess of noradrenaline the diastolic pressure is very high and the heart-rate usually slow and forceful owing to vagal reflexes from the aortic arch. These signs are reinforced by the almost invariable profuse sweating and cold clammy skin. Because of albuminuria some cases suggest pyelonephritis or nephritis, and others diabetes because of glycosuria and a mildly diabetic type of glucose-tolerance curve which disappears after operation. Anxiety neurosis and thyrotoxicosis must be differentiated because of the tremor, tachycardia, palpitations, and sweating, and a moderate elevation of the B.M.R. may be confusing. The constant nature of the attacks may help to refute a diagnosis of neurosis. Should headache predominate, an intracranial tumour may also seem a possibility.

Considerable fluctuation in the blood-pressure may be seen in patients with essential hypertension, sometimes before the basal level has become permanently elevated, and mere lability of the blood-pressure is not diagnostic of a phæochromocytoma. Occasionally patients present with an abdominal mass of uncertain nature and are found to have hypertension, the significance of which is ignored until a laparotomy reveals the origin of the tumour or there is sudden death. Gilliland and Daniel (1951) reported a case presenting as a surgical emergency in which there was hæmorrhage into the tumour and peritoneum.

It is impossible to describe in detail or to analyse all the symptoms and signs produced by these fascinating tumours. The reason for such severe sweating when sweat-glands are largely cholinergic is uncertain, and the cause of the thyroid enlargement which sometimes occurs during an attack, or when noradrenaline is infused into certain normal subjects, is obscure. Of course, when the hypertension has been severe for some time renal factors contribute to its maintenance, and with a diastolic pressure of over 140 mm. Hg widespread arteriolar damage may lead to a malignant termination.

Though surgical cure at this late stage is less likely, operation is quite justifiable, for malignant hypertension is an expression of the severity and acuteness of the hypertension and is not necessarily irreversible.

It is possible that a renal factor may account for the continued mild post-operative hypertension in our second case, a not unusual occurrence in these patients.

Goldenberg, Aranow, Smith, and Faber (1950) found that 12 out of 18 patients who had tumours removed still had abnormally high blood-pressures.

The literature which has accumulated in the last decade is extensive, but for more complete descriptions of the clinical picture the papers of McKeith (1944), Cahill and Aranow (1949), Walton (1950), and Hamilton, Litchfield, Peart, and Sowry (1953) may be consulted.

PATHOLOGICAL ASPECTS

These tumours are usually benign and may arise from any chromaffin tissue in the body, though it is rare to find them outside the abdomen. The adrenal medulla is most often their source of origin, but they can also arise from remnants of the organs of Zuckerkandl in the para-aortic region. Bierman and Partridge (1951) found that 20 per cent of 208 cases in the literature were outside the adrenals, though not all may be endocrinologically active. Two or more tumours were present in 15 of 176 reported cases according to Calkins and Howard (1947), and a small proportion of patients seem to grow second tumours after the first has been removed and all diagnostic tests have become negative.

Their weight varies from a few grammes to several pounds, and their pharmacological activity bears no direct relation to their mass. Histologically their appearance is similar to that described in our case reports, and it is from their staining properties with chromates that they take their name—the dark-coloured tumours. They are usually encapsulated and the adrenal cortex may be considerably compressed. The histological picture is variable, the cells being large, polyhedral, and at times multinucleated, separated by many vascular channels. These cells contain neutral fat and anisotropic lipoids and at times appear to invade the veins.

Characteristic staining reactions are given by modifications of the Otaga-Otaga chromaffin stain and Schmorl's giemsa stain for adrenaline.

The majority are benign, and apparent invasion of blood-vessels does not always indicate malignancy, as pointed out by Blacklock, Ferguson, Mack, Shafar, and Symington (1947) who reviewed the pathology thoroughly. They cited the case of a normotensive woman in whom there was a massive recurrence of growth following operation.

Cross and Pace (1950) also recorded the history of a middle-aged man who had metastases in the spine and neurological symptoms, but malignant phæochromocytomas are in fact rare.

Their pharmacological properties are of much more importance, the average phæochromocytoma containing sufficient adrenaline to make over 500 ml. of liquor adrenaline B.P.

PHARMACOLOGY

All the signs and symptoms are attributable to an excess of circulating adrenaline, either liberated continuously or paroxysmally. The recent elucidation of the pharmacology of adrenaline has emphasized the difference between adrenaline and its precursor, noradrenaline. In 1910 Barger and Dale distinguished the two, but no correlation with the physiological observations on the nervous system was apparent. The possibility of inhibitor and excitor 'sympathins' was postulated, the excitor conceivably being noradrenaline. The studies of von Euler (1951, a, b), Gaddum and Goodwin (1947), and West (1947) in the last few years have proved that noradrenaline is released from the spleen and adrenal after sympathetic nerve stimulation rather than adrenaline, confirming the earlier hypotheses. It is now known that the normal adrenal medulla contains a mixture of 80 per cent adrenaline and about 20 per cent of its unmethylated precursor noradrenaline.

In phæochromocytomas the tumour tissue seems unable to transmethylate noradrenaline, the proportion of which rises to over 90 per cent of all the pressor substances, as first shown by Holton (1949). It is of interest that West, Shepherd, and Hunter (1951) found an increased proportion in fœtal adrenals, the ratio returning to normal within the first few months of life. The symptoms and signs will to some extent depend on the ratio present in the tumour since the actions of each differ. The main variations are summarized in *Table I*.

Table I.—VARIATIONS IN HUMAN RESPONSE TO INTRAVENOUS INFUSIONS OF *l*-ADRENALINE AND *l*-NORADRENALINE

	Adrenaline	*Noradrenaline*
Blood-pressure { Systolic	Elevated +	Elevated + +
Blood-pressure { Diastolic	Little or no rise	Elevated +
Pulse-rate	Rapid	Slowed reflexly
Cardiac output	Increases	Falls
Arterioles { Skin	Constricted +	Constricted + +
Arterioles { Muscle	Dilated	Constricted
Peripheral resistance	Decreased	Increased
Blood-sugar	Elevated	Little effect
Tremor	Present	Absent

The assay on the tumour from *Case* 1 exhibiting paroxysmal hypertension gave figures of 1·6 mg. *l*-noradrenaline and 0·1 mg. *l*-adrenaline per gramme of tumour tissue. In *Case* 2 with sustained hypertension the quantities were 9·8 mg. *l*-noradrenaline

and 1·7 mg. *l*-adrenaline. The total adrenaline content in the average-sized phæochromocytoma is therefore very large and von Euler (1951, a) estimated that up to 2 mg. per hour was liberated, the equivalent of 0·5 μg. per kilo body-weight a minute. A few weeks after operation we infused noradrenaline into out first patient at a rate of up to 34 μg. a minute, his blood-pressure rising to 245/135, at which point he developed headache and pounding of the heart of a similar though less severe nature than in his attacks.

His tumour probably secreted noradrenaline at a slightly higher rate, but our figures are in fair agreement with those of von Euler based on calculations from urinary excretion. What factors are concerned in the sudden liberation of adrenaline is uncertain save in those cases in which movement, trauma, or massage stimulates the tumour directly.

The pharmacology of noradrenaline and of the phæochromocytomas has been dealt with clearly by von Euler (1951, b) and by Goldenberg (1951).

DIAGNOSTIC TESTS

These may be grouped under the headings shown below (*Table II*).

Table II.—SUMMARY OF DIAGNOSTIC TESTS

1. *Provocation of Hypertension:*—
   Massage to the loins or tumour; change of posture.
   Intravenous histamine, 0·025 mg.
   Tetraethylammonium bromide, 250 to 400 mg. I.V.
   Mecholyl, 0·25 mg. S.C.
2. *Adrenaline Antagonists causing Hypotension:*—
   Regitine, 5 mg. I.M.I.
   Piperoxane (Benzodioxane), 10 to 20 mg. I.V.
   Dibenamine, 250 to 500 mg. I.V.
3. *Detection of Pressor Amines:*—
   Urinary adrenaline assay (biological or chromatographic).
   Plasma-adrenaline.
   Plethysmograph and skin temperature studies (indirect evidence).
4. *Localization of Tumour:*—
   Intravenous pyelogram.
   Perirenal oxygen insufflation.
   Tomography.

Not all of these tests are without risk and it is by no means kind or necessary to subject the patient to a pharmacological parlour game. Those that are of the greatest value in order of importance are, apart from localization, assay of the urinary pressor amines and the regitine test, with the piperoxane and histamine tests of less value. The tetraethylammonium bromide (TEAB), mecholyl and dibenamine tests are unreliable and dangerous.

Urinary Pressor Amines.—The normal adrenal medulla contains about 80 per cent adrenaline and 20 per cent noradrenaline, the same proportion being present in liquor adrenaline of animal origin, but in these tumours the proportions are reversed and noradrenaline may comprise 95 per cent of the total pressor amines.

In the normal adult a small quantity of adrenaline and other pressor material derived partly from the adrenal medulla and partly from the sympathetic nervous system is excreted in the urine in spite of its rapid destruction in the body by amine oxidase. Following the observations of Richter (1940), both von Euler (1951, a) and Goldenberg (1951) have shown that the normal daily excretion of pressor amines is about 50 μg. daily, some 30 μg. as *l*-noradrenaline and about 10 μg. as *l*-adrenaline. If an adrenaline-producing tumour is present there is a significant increase. von Euler (1951 a) considers levels of above 130 μg. diagnostic, and has reported a daily excretion of 1800 μg. in some patients. The reliability of biological assay has been confirmed by Hamilton and others (1953); it is diagnostically essential in all uncertain cases and to ascertain whether a second tumour is present after operation should the blood-pressure remain elevated.

About 500 ml. of urine should be collected and acidified with 2 ml. of concentrated HCl to keep the *p*H about 4, the specimen being kept in the cool in a dark bottle and extracted according to von Euler's technique. The assay is carried out biologically, and it has been suggested that direct injection of buffered urine into a cat will produce a significant elevation of blood-pressure should a tumour be present. Specimens from *Case* 2 collected without relation to a paroxysm, contained 599 μg. and 780 μg. noradrenaline, and 3 μg. and 24 μg. adrenaline, per litre of urine. There seems to be no correlation between the proportion of each excreted and the clinical picture.

The Regitine Test.—This diphenylamine derivative of the imidazoline series has properties antagonistic to adrenaline, and its pharmacology has been reviewed by Gifford, Roth, and Kvale (1952). After investigating 259 hypertensive patients they concluded that regitine was not toxic and that fewer false positive results were obtained if the intramuscular route was followed and the dose limited to 5 mg. Two-thirds of their patients had a fall in blood-pressure averaging 20 mm. systolic and 14 mm. diastolic. It is only in cases of phæochromocytoma that a sudden and sustained fall of 35 mm. or more follows, as in our second case when there was a drop from 300/190 to 130/80 within 25 minutes (*Fig.* 210). Between the paroxysms the resting blood-pressure also fell from 190/120 to 120/80 (*Fig.* 211). The other patient was given 7 mg. intravenously during a mild paroxysm, the blood-pressure falling from 250/138 to 168/90, followed by a slow rise to 200/105 after fifteen minutes. As confirmed by Emlet, Grimson, Bell, and Orgain (1951) and by Iseri, Henderson, and Derr (1951), the regitine test is a simple and reliable diagnostic test, though undoubtedly less certain than estimation of the urinary pressor amines.

Piperoxane Test.—The adrenaline antagonists were evolved by Fourneau in 1933 but were put to no practical application until Goldenburg, Snyder, and Aranow (1947) described the use of piperidylmethyl benzodioxane as a diagnostic agent in phæochromocytomas. It is usual to inject 0·25 mg. per kilo body-weight within two minutes, an average dose being between 10 and 20 mg. As in our first patient a positive result is indicated by a fall of over 30 mm. Hg, but false positive results are too often seen in essential hypertensives, particularly when there is renal impairment.

Other unsatisfactory points are the frequency of negative results even when a tumour is subsequently removed, as reported by Taliaferro, Adams, and Haag (1949), Place (1951), and others, the high incidence of side-effects such as tachycardia, flushing, dizziness, and dyspnœa, plus an alarming tendency to a paroxysmal rise in blood-pressure sometimes leading to encephalopathy (Wilkins, Greer, Culbertson, Halperin, Litter, Burnett, and Smithwick, 1950).

In view of these findings piperoxane should be used with caution and not at all in uræmic patients or when urinary adrenaline assays are feasible.

Intravenous Histamine Test.—When a very small dose of histamine, such as 0·025 mg., is slowly given intravenously to the normal subject there is a fall in peripheral resistance due to capillary paralysis and a fall in blood-pressure. Experimentally,

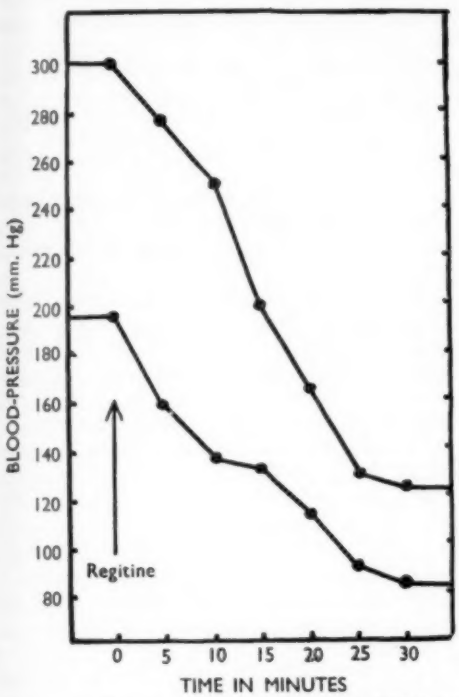

FIG. 210.—*Case* 2. Positive regitine test during paroxysma hypertension (5 mg. intramuscularly).

however, Burn and Dale (1926) noted that the blood-pressure might rise in certain animal preparations, and it has been shown later that perfusion of isolated adrenals with dilute histamine is followed by liberation of adrenaline.

Roth and Kvale (1945) found that when an adrenaline-producing tumour was present a hypertensive response resulted in contrast to the normal fall in blood-pressure, due presumably to direct stimulation of the adrenals. The dose should be diluted in 5 ml. of water, the blood-pressure being recorded carefully as the elevation may last only a few minutes. Though of well-established value in cases with a normal blood-pressure between paroxysms, it is not without risk; extreme hypertension may follow as in the case reported by Kositchek and Rabwin (1950) when there was a rise to above 300 mm. systolic. False negative tests have been seen by many authors including Aranow (1950), Shapiro, Baker, Hoffman, and Ferris (1949), Calkins, Dana, and Howard (1951) and others.

The first patient was given 0·025 mg. on one occasion, the blood-pressure rising from 175/108 to 202/130 after six minutes, but on a second occasion 0·05 mg. had no pressor effect.

Other Tests.—The three other tests already mentioned do not usually provide much useful information. Intravenous TEAB appears to have a stimulating effect on the tumour and, as observed by La Due, Murison, and Pack (1948), a pressor response is elicited in contrast to the normal short-lived hypotension. There was no change in the blood-pressure after 250 mg. in the first patient, but possibly 400 mg. might have been effective.

Many false positive results have been recorded (Bartels and Cattell, 1950; Bierman and Partridge,

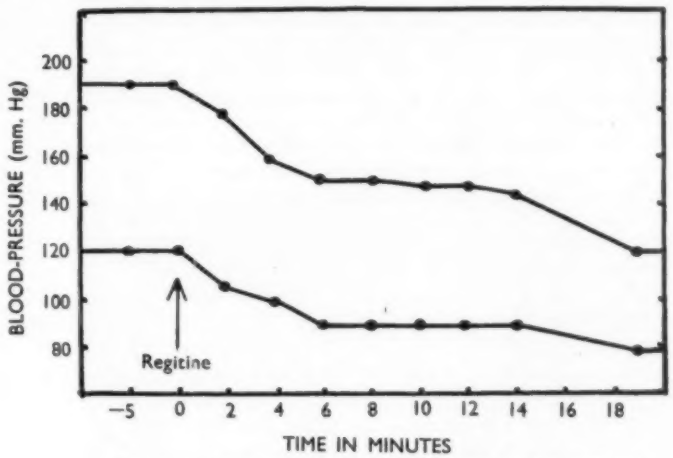

FIG. 211.—*Case* 2. Response to regitine during sustained hypertension (5 mg. intramuscularly).

1951), and false negatives by Iversen (1952) and by Beyer, Ross, Wiebelhaus, Waller, and Schuchardt (1951).

Similarly, the mecholyl test of Guarneri and Evans (1948) is unreliable, a positive result after a subcutaneous dose of 0·25 mg. being indicated by a pressor response of 20 mm. or more. Once again, misleading negative results are common, and have been recorded by Shapiro, Baker, Hoffman, and Ferris (1949) and by Anderson, Rolufs, and Doerner (1952).

Dibenamine is very toxic, causing restlessness, nausea, vomiting, and confusion in many cases, and as shown by Haimovici (1951) the blood-pressure often falls in essential hypertensives.

Plethysmography, skin temperature, heat elimination studies are not practical in most hospitals and cannot be relied on absolutely.

DISCUSSION

Surgical removal must be attempted whenever a tumour is found to be present and exploratory laparotomy may be justified if the clinical picture is strongly suggestive of a phæochromocytoma.

The most reliable diagnostic test is undoubtedly the urinary pressor amine excretion, and we have seen two cases with a suspicious history, in which the urinary assays were normal, which have been explored surgically with negative findings. With such wide variations in the clinical manifestations its value cannot be overemphasized.

Localization of the tumour may be difficult in obese patients in spite of adequate intravenous pyelograms, and the perirenal insufflation of oxygen is not to be recommended in severely ill patients in case a paroxysm of hypertension should result. We consider that a preliminary laparotomy is reasonable

in uncertain cases, the tumour being removed through a loin incision at the same operation, or later if the patient's condition is unsatisfactory. In this way tumours in the para-aortic region may be located and dealt with, inspection being denied in the the approach from the loin. The high mortality associated with operation a few years ago was wrongly attributed to an excess of adrenaline liberated during removal rather than to a lack to be treated by replacement. The hypertension which develops as the tumour is approached and palpated is seldom fatal, but the rapid and inevitable fall in blood-pressure to shock levels immediately after removal is a common cause of death.

The pre-operative use of 5–10 mg. of regitine prevents excessive hypertension and may reduce the rebound hypotension without necessarily impairing the response to noradrenaline. The most important aid to recovery is the immediate use of noradrenaline intravenously to keep the blood-pressure at about 120/80, and for this purpose between 30 and 100μg. a minute may be necessary. In both our patients noradrenaline had to be continued for over eighteen hours in decreasing doses. It must be emphasized that liquor adrenaline B.P. is useless. As with other operations on the adrenals, preparation with cortisone for a few days before and after removal may assist recovery, which in both patients was somewhat slower than might be expected in operations of comparable technical magnitude.

SUMMARY

The histories of two patients with hypertension due to phæochromocytomas are recorded in both of whom surgical removal was successful.

The pharmacological basis of the symptoms and signs has been considered and the importance of noradrenaline in their production has been emphasized.

Tests of special value in the diagnosis of phæochromocytomas have been reviewed and evaluated.

Some points of relevance in the surgical care of these patients have also been discussed.

We are particularly indebted to Dr. Monica Mann, of the School of Pharmacy, University of London, who carried out the urinary adrenaline assays on these and other patients and has so willingly given advice. We must also acknowledge the help given by Dr. R. S. Bruce Pearson and Dr. S. Nevin, and Professor H. A. Magnus.

REFERENCES

ANDERSON, W. H., ROLUFS, L. S., and DOERNER, A. A. (1952), *Amer. Heart J.*, **43**, 252.
ARANOW, H. (1950), *Med. Clin. N. Amer.*, **34**, 757.
BARGER, G., and DALE, H. (1910), *J. Physiol.*, **41**, 19.
BARTELS, E. C., and CATTEL, R. B. (1950), *Ann. Surg.*, **131**, 903.
BEER, E., KING, F. H., and PRINZMETAL, M. (1937), *Ibid.*, **106**, 85.
BEYER, K. H., ROSS, C. A., WIEBELHAUS, V. D., WALLER, W. S., and SCHUCHARDT, G. S. (1951), *Ann. intern. Med.*, **35**, 117.
BIERMAN, H. R., and PARTRIDGE, J. W. (1951), *New Engl. J. Med.*, **244**, 577.
BLACKLOCK, J. W. S., FERGUSON, J. W., MACK, W. S., SHAFAR, J., and SYMINGTON, T. (1948), *Brit. J. Surg.*, **35**, 179.
BURN, J. H., and DALE, H. H. (1926), *J. Physiol.*, **61**, 185.
CAHILL, G. F., and ARANOW, H. (1949), *Ann. intern. Med.*, **31**, 389.
CALKINS, E., DANA, G. W., and HOWARD, J. E. (1951), *J. Amer. med. Ass.*, **145**, 880.
— — and HOWARD, J. E. (1947), *J. clin. Endocrin.*, **7**, 475.
CROSS, G. O., and PACE, J. W. (1950), *J. Amer. med. Ass.*, **142**, 1068.
EMLET, J. R., GRIMSON, K. S., BELL, M. D., and ORGAIN, M. S. (1951), *Ibid.*, **146**, 1383.
VON EULER, U. S. (1951, a), *Ann. Surg.*, **134**, 929.
— — (1951, b), *Brit. med. J.*, **1**, 105.
GADDUM, J. H., and GOODWIN, L. G. (1947), *J. Physiol.*, **105**, 357.
GIFFORD, R. W., ROTH, G. M., and KVALE, W. F. (1952), *J. Amer. med. Ass.*, **149**, 1628.
GILLILAND, I. C., and DANIEL, O. (1951), *Brit. med. J.*, **2**, 275.
GOLDENBERG, M. (1951), *Amer. J. Med.*, **10**, 627.
— — ARANOW, H., SMITH, A. A., and FABER, M. (1950), *Arch. intern. Med.*, **86**, 823.
— — SNYDER, H. C., and ARANOW, H. (1947), *J. Amer. med. Ass.*, **135**, 971.
GUARNERI, V., and EVANS, J. A. (1948), *Amer. J. Med.*, **41**, 806.
HAIMOVICI, H. (1951), *Angiology*, **2**, 531.
HAMILTON, M., LITCHFIELD, J. W., PEART, W. S., and SOWRY, C. S. C. (1953), *Brit. Heart J.*, **15**, 241.
HOLTON, P. (1949), *J. Physiol.*, **108**, 529.
ISERI, L. T., HENDERSON, H. W., and DERR, L. T. (1951), *Amer. Heart J.*, **42**, 129.
IVERSEN, K. (1952), *Acta med. scand.*, **142**, 1.
KOSITCHEK, R. J., and RABWIN, M. H. (1950), *J. Amer. med. Ass.*, **144**, 826.
LABBÉ, M., TINEL, J., and DOUMER, H. (1922), *Bull. Soc. méd. Hôp. Paris*, **46**, 982.
LA DUE, J. S., MURISON, P. J., and PACK, G. T. (1948), *Ann. intern. Med.*, **29**, 914.
MCKEITH, R. C. (1944), *Brit. Heart J.*, **6**, 1.
PINCOFFS, M. C. (1929), *Trans. Ass. Amer. Phys.*, **44**, 295.
PLACE, V. A. (1951), *J. Amer. med. Ass.*, **146**, 1227.
RICHTER, D. (1940), *J. Physiol.*, **98**, 361.
ROTH, G. M., and KVALE, W. F. (1945), *Amer. J. med. Sci.*, **210**, 653.
SHAPIRO, A. P., BAKER, H. W., HOFFMAN, M. S., and FERRIS, E. B. (1949), *J. Lab. clin. Med.*, **34**, 1751.
SMITHWICK, R. H. (1951), *Surgical Measures in Hypertension.* Illinois: C. C. Thomas.
TALIAFERRO, I., ADAMS, R. A., and HAAG, H. B. (1949), *J. Amer. med. Ass.*, **140**, 1271.
WALTON, J. N. (1950), *Lancet*, **2**, 966.
WEST, G. B. (1947), *J. Physiol.*, **106**, 418.
— — SHEPHERD, D. M., and HUNTER, R. B. (1951), *Lancet*, **2**, 966.
WILKINS, R. W., GREER, W. E. R., CULBERTSON, J. W., HALPERIN, M. H., LITTER, J., BURNETT, C. H., and SMITHWICK, R. H. (1950), *Arch. intern. Med.*, **86**, 51.

VESICO-INTESTINAL FISTULA AND CROHN'S DISEASE

By R. J. WILLIAMS
CARDIFF ROYAL INFIRMARY

DURING the past three years 7 cases of vesico-intestinal fistula and 6 cases of Crohn's disease, 1 of which was associated with vesico-intestinal fistula, were observed at Cardiff Royal Infirmary and the East Glamorgan Hospital, Church Village, and it was thus deemed of interest to examine the literature of the past twenty years, during which period regional ileitis has been frequently observed, for a reassessment of the aetiology of fistulæ between the bladder and alimentary tract. Previously reported larger series were reviews not of cases experienced by individual surgeons or clinics, but of all recorded cases, single or multiple. This system of review seemed to favour the fistulæ of inflammatory origin, as there is little doubt that these have been considered of much greater interest than those of congenital, traumatic, and neoplastic origin, and have been reported with greater frequency. It was decided, therefore, that in order to gain a more accurate picture of the aetiology it was necessary to collect together the several complete series observed personally by individual surgeons. In this way 148 cases of vesico-intestinal fistulæ have been gathered. In addition careful search was made in the literature from 1920 onwards for cases of vesico-intestinal fistula which might have been due to regional ileitis. A total of 17 such cases has been found.

CASE REPORT

Vesico-intestinal fistula due to regional ileitis. The patient was a young woman whose history is best given in chronological order.

1947: At the age of 19 years following spasmodic pain in the right iliac fossa she underwent appendicectomy; the appendix being found normal.

1949: She commenced to experience diarrhœa, passing frequent watery stools which, however, never contained pus or blood. There were frequent pyrexial attacks.

1950: She was admitted to hospital on account of these symptoms, to which were now added lower abdominal colic and loss of weight. Her general condition was fair, she showed occasional spikes of elevated temperature. There was some tenderness in the right iliac fossa and on bimanual examination a small mass could be felt in the right side of the pelvis. This was thought to be tubal in origin. Hæmoglobin 59 per cent. Urine, no abnormality. Barium enema and sigmoidoscopy revealed no abnormality. A course of streptomycin and P.A.S. was started on the assumption that the pelvic mass was a tuberculous pyosalpinx.

1951: Early in the year she developed marked frequency of micturition, passing water 13–14 times during the day and 3–4 times at night. The urine at no time contained blood, but was occasionally brown in colour. Diarrhœa was not pronounced. Loss of weight continued. She was admitted to hospital in June. Her general condition was very poor indeed: her temperature showed daily elevation. She was pale and wasted and a large firm mass could be felt arising from the right side of the pelvis to halfway between the pubis and the umbilicus. Hæmoglobin 63 per cent. Intravenous pyelography showed normal renal outlines, but the vault of the bladder exhibited a filling defect, mainly to the right of the midline (*Fig.* 212). Nothing could be seen on cystoscopy because of bleeding. A cystogram showed dye lying both in a cavity above the bladder and in the sigmoid (*Figs.* 213, 214), this cavity it transpired later was terminal ileum.

On July 24 laparotomy was performed following blood transfusion, colonic lavage, and a course of intestinal chemotherapy. The mass previously palpated was found

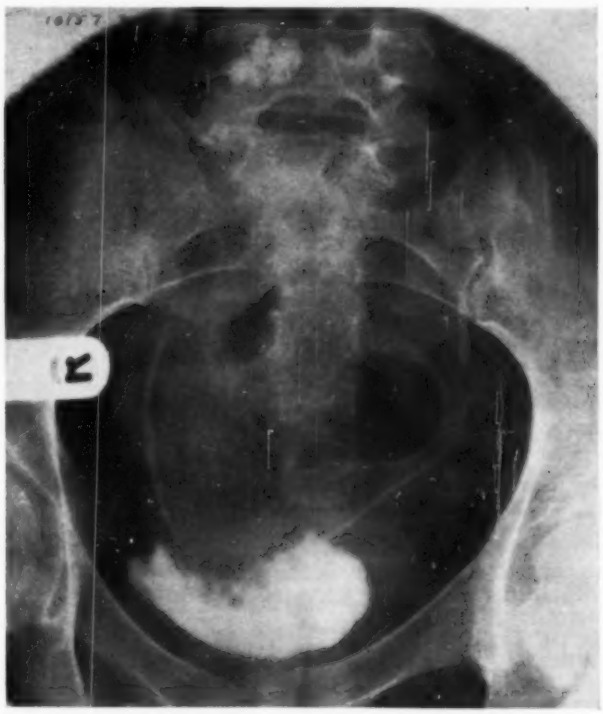

FIG. 212.—Intravenous pyelogram. The excretion cystogram shows a large filling defect of the vault of the bladder mainly to the right of the midline. The ureters are normal in calibre and the concentration of dye is good.

to consist of thickened coils of terminal ileum matted one to another and adhering to the anterior abdominal wall, bladder, and rectosigmoid. Diagnosis of Crohn's disease with ileorectal and ileovesical fistula was then made: the length of ileum intervening between the two fistulæ was some 3 in. Adhesiotomy was performed and the fistulæ were resected. The terminal ileum (about 2 ft.), cæcum, and proximal ascending colon were resected well clear of the macroscopic limits of involvement: the stump of ascending colon was closed and end-to-side ileocolic anastomosis performed. The hole left in the bladder was closed in two layers with great difficulty owing to the cartilaginous consistency exhibited by the entire vesical vault: then to ensure adequate drainage cystotomy was performed through the anterior wall of the viscus. The hole in the rectosigmoid was repaired by suturing it transversly in three layers after preliminary paring of the edges. The rectosigmoid itself appeared free from any actual granuloma. After the establishment of a left inguinal colostomy the abdomen was closed in layers with drains to the ileocolic anastomosis, the pouch of

Douglas, and the prevesical space. The patient developed paralytic ileus and also pyelitis. Both responded well to treatment. The suprapubic cystotomy was abandoned after fourteen days and the patient discharged from hospital on the twenty-second day after operation. Three months later the inguinal colostomy was closed and the patient had gained over 2 st. in weight. Intravenous pyelography performed since showed nothing abnormal. Indurated thickening of the resected portion of gut was observed in the last 18 in. of terminal ileum and in the cæcum adjacent to the ileocæcal valve. Microscopical examination showed giant-cell granuloma with no necrosis of the follicles.

FIG. 213.—Injection cystogram. Sodium iodide injected through the catheter depicted failed to outline the bladder but revealed a cavity above the bladder communicating with the rectosigmoid. This cavity proved to be constituted by the terminal ileum. Left oblique view.

FIG. 214.—As *Fig.* 213. Right oblique view.

AETIOLOGY

For the purposes of analysis, in addition to my own series the cases observed by the following authors are gathered together (*Table II*).

Thus altogether 148 cases are examined. In the group are included several cases in which the fistula actually occurred between the posterior urethra and the alimentary tract. In these instances, however, the fistula was so near the bladder, and the behaviour of the fistula so similar, that most authors include these fistulæ in the grouping of vesico-intestinal fistula. I have, however, excluded two cases of Wilhelm's series, both following urethral instrumentation, as these in all probability were below the sphincter urethræ in the anterior urethra. The average age in the series as a whole is over fifty years.

It has not been possible to analyse the sex distribution in the series as a whole, but out of 101 cases, 76 were in males and 25 in females;

Table I.—OTHER CASES OF VESICO-INTESTINAL FISTULA SEEN AT THE CARDIFF ROYAL INFIRMARY AND THE EAST GLAMORGAN COUNTY HOSPITAL

No.	Sex	Age	Type of Fistula	Aetiology	Treatment
2	Male	64 yr.	Rectovesical	Prostatectomy	Bladder drainage
3	Male	17 yr.	Rectovesical	Perforating wound of rectum	Drainage of bladder. Colostomy
4	Male	44 yr.	Vesicosigmoid	Carcinoma of sigmoid	Colostomy
5	Male	2 d.	Recto-urethral	—	Colostomy. Mobilization of rectum to perineum. Division of fistula
6	Male	49 yr.	Rectovesical	T.B. cystitis, stone	Nil, uræmic
7	Male	63 yr.	Rectovesical, vesico-urethral	Carcinoma of bladder	Nil

The disease progress in this case was presumably from an acute onset in 1947, when during an episode of acute regional ileitis the appendix was removed; this was followed in 1949 by supervention of a chronic phase, with gradual development of an ileo-rectal fistula. Ileovesical fistula was established probably early in 1951.

vesico-intestinal fistula is thus three times more common in males.

Vesico-intestinal fistulæ may be gathered from the viewpoint of aetiology into four main groups—congenital, traumatic, inflammatory, and neoplastic.

Table II.—Other Reported Cases

Authors	*No. of Cases*
Higgins (1936)	35
Balch (1936)	19
Ewell and Jackson (1941)	11
Willan (1933)	6
Morrissey (1941)	5
Forbes (1940)	5
Barnes and Hill (1942)	14
Lazarus and Marks (1943)	5
Wilhelm (1944)	16
Ormond, Best, and Klinger (1949)	25

The gross analysis of the cases under consideration is given in *Table III*.

Congenital Fistulæ.—Six cases are congenital, an incidence of 4 per cent. All were associated with imperforate anus, which is an invariable finding.

Table III.—Aetiological Details of 148 Cases

Type	Individual Numbers	Series Total
Congenital	—	6
Traumatic		22
Perforating wound	1	
Post-operative	19	
Foreign-body	1	
Radiotherapy	1	
Inflammatory		51
Meckel's diverticulum	1	
T.B. enteritis	3	
Regional ileitis	8	
Appendicitis	4	
T.B. cystitis	2	
Diverticulitis	23	
Diverticulum of bladder	2	
Vesical calculus	3	
Periprostatic or perirectal abscess	4	
Actinomycosis	1	
Neoplastic		64
Carcinoma of bladder	10	
Carcinoma of prostate	1	
Carcinoma of ovary	2	
Carcinoma of cervix	5	
Carcinoma of vagina	1	
Carcinoma of cæcum	1	
Carcinoma of sigmoid	19	
Carcinoma of rectosigmoid	5	
Carcinoma of rectum	20	
Uncertain		5

Ladd and Gross (1948) classify this anomaly into four groups—namely: Type 1, where there is a stenosis of a few centimeters above the anus; Type 2, imperforate anus with membranous obstruction; Type 3, imperforate anus where the rectal pouch ends blindly some distance above the anus; and Type 4, where the anus and anal pouch are present but the rectum ends blindly in the sacral hollow. In their series of 214 cases of imperforate anus, 117 had fistulæ between the rectum and urinary tract or perineum. None of these was associated with the Type 4 anomaly.

There is a marked male predominance, and the fistula opens in one of three situations: (1) The trigone of the bladder; (2) The prostatic urethra; (3) The membranous urethra.

The case observed at the Cardiff Royal Infirmary had a Type 3 ano-rectal anomaly and a recto-urethral fistula opening into the prostatic urethra.

Traumatic Fistulæ.—Twenty-two cases are analysed, an incidence in the total series of 14·6 per cent, and 19 of these followed operation.

Very few occur as the result of civil accident or war wound. Both cases in my personal series were seen at the East Glamorgan County Hospital. One followed a transvesical enucleation of the prostate (*Case* 2), but the other (*Case* 3) was due to civil injury—a youth accidentally fell astride some pointed iron railings; one spike perforated his buttock, entered the anus, and passed through the anterior rectal wall, perforating the trigone of the bladder. In two instances known to me where the anterior wall of the rectum has been perforated by a blunt object the bladder has been pushed forward and the pelvic peritoneum upward so that a large extra-peritoneal pelvic hæmatoma rather than a traumatic rectovesical fistula has resulted. Thus in a personal case where a man had fallen off a cart and on to the handle of a muck-fork which entered his anus, a gross perforation of the anterior rectal wall just below the trigone of the bladder was present but the bladder was not perforated and the floor of the pouch of Douglas was elevated to the plane of the pelvic brim by a vast hæmatoma. Another factor governing the occurrence of fistulæ in perforating injuries of the anterior rectal wall is probably the state of fullness of the bladder. Only 1 per cent of perforating war wounds of the bladder were complicated by vesico-intestinal fistula (Robinson, Culp, Suby, Reiser, and Mullenix, 1946).

In former days the operation of perineal lithotomy was commonly followed by rectovesical or recto-urethral fistula (Duff, 1937); now, however, operations on the prostate, whether by the suprapubic, perineal, or perurethral routes, and the uterus are the common sources of injury. Resection of the bladder-neck for bladder-neck stenosis or following prostatectomy may be associated with direct injury to the rectum or may be followed by cellulitis and abscess formation in the rectovesical septum, the abscess rupturing both into bladder and rectum, and causing a fistulous communication. In at least 10 cases out of the 22 traumatic fistulæ of the larger series, fistulæ followed prostatectomy. Operations about the vaginal vault are also common sources of injury to the bladder and rectum, individually or together. Many of the post-operative fistulæ are anatomically recto-urethral but open so high that they are immediately adjacent to the bladder-neck and virtually vesical.

Inflammatory Fistulæ.—Inflammatory lesions were responsible in 51 cases, or 33 per cent of the total.

Although the appendix is not uncommonly the primary source of fistula formation (Pemberton, Pool, and Miller, 1940), I have found only 2 cases of ileovesical fistula arising from a Meckel's diverticulum; only one is included in this series, but the other, reported by Lange (1949), is of great interest as the patient, presenting with hæmaturia, had a bleeding ulcer in a Meckel's diverticulum associated with a bladder fistula. Tuberculous enteritis was responsible for only 3 cases of the present collected

series; of these, 2 were rectovesical fistulæ due to tuberculous enterocolitis (Ormond, Best, and Klinger, 1949), and only 1 case was ileovesical (Willan, 1933).

Four cases were due to appendicitis. The usual cause is acute suppurative appendicitis, but it is interesting to note that in the discussion on Balch's (1936) paper Mackenna described 3 cases of appendicovesical fistula, in 2 of which tubercle bacilli were isolated from the urine. The appendix may be directly adherent to the bladder or may communicate with it through an abscess cavity, the so-called appendico-pyovesical type, which of course is the aftermath of an appendix abscess which ruptures into the bladder.

The commonest inflammatory lesion responsible for vesico-intestinal fistula is diverticulitis (Rankin, Bargen, and Buie, 1932; Mayfield and Waugh, 1949), a disease occurring predominantly in males of the sixth decade. This accounts for 23 cases, or 15 per cent of the present series. Rankin and Brown (1930) consider that diverticula of the large intestine are present in 1 per cent of the population. In Sprigg's (1927) series of 158 cases of diverticulosis, 73 per cent of diverticula occurred in the sigmoid. Telling and Sruner (1916) found that in 280 cases of diverticulitis the sigmoid was adherent to the bladder in 33 cases. Norbury (1938) had pointed out that for this reason bladder symptoms are not uncommon in diverticulitis even in absence of fistula; but at the same time the frequency of sigmoidovesical adhesions accounts for the comparative frequency of diverticulitis as a cause of fistula.

Two cases were due to tuberculous cystitis, and one of these was observed at Cardiff Royal Infirmary. The mechanism was probably penetration of the rectum by a tuberculous ulcer originating on the trigone of the bladder or rupture of a perivesical abscess into the rectum. Two cases were due to diverticulum of the bladder; vesical diverticula often lie deep in the pelvis between the bladder and rectum. They are seats of chronic sepsis and become closely adherent to surrounding structures; abscess formation and penetration of the rectum results in fistula formation.

Three cases were due to vesical calculus. Whilst there is no doubt that a vesical calculus may ulcerate into the rectum and cause a fistula, calculus may also form in the bladder infected from a fistula, and a certain note of caution is necessary in ascribing a fistula to a calculus before another cause has been excluded.

Apart from 5 cases, 4 due to periprostatic or perirectal abscess and 1 to actinomycosis, the remainder of the inflammatory fistulæ were due to Crohn's disease. In the series of Cripps (1888), Pascal (1899), and Sutton (1921), syphilis, typhoid, gonorrhœa, and amœbiasis are listed as causes. These are all diseases which at present are seen with decreasing frequency in their advanced stages. In the cases ascribed to syphilis in the old series the lesions responsible might well in many instances have been non-syphilitic, occurring coincidentally in syphilitic subjects. Gonorrhœa cannot be so dismissed, for in Sutton's 34 cases of vesicosigmoid fistula (1906–20) acute salpingitis was an aetiological factor in 26 per cent.

Typhoid fever has become increasingly uncommon during the past forty years, and no instances of fistula attributable to this are seen in the series under review. No fistulæ due to amœbiasis are noted, although since the 1939–45 war the condition is not infrequently encountered. Rebori (1944) has recently reported one case of vesicosigmoid fistula of amœbic origin.

Of the 51 cases of inflammatory vesico-intestinal fistula, 7 arise from the urinary tract and 40 from the alimentary tract. In the latter group small-intestine lesions are responsible for 10, appendicitis for 4, and large-intestine inflammatory disease for 26 cases.

Crohn's Disease.—"Fistula formation is the most constant clinical and pathological phenomenon in ileitis" (Crohn).

The number of cases of bladder fistula in relation to the number of cases of Crohn's disease reviewed is noted in *Table IV*.

Table IV.—BLADDER FISTULA IN RELATION TO CROHN'S DISEASE

Author	*Cases of Crohn's Disease*	*Cases of Bladder Fistula*
Crohn (1949)	298	4
Clark and Dixon (1939)	44	1
Pugh (1945)	17	1
Author	6	1

In the above 365 cases of Crohn's disease, 7 bladder fistulæ are reported. In addition to these, in the literature appears 8 other definite cases and 2 probable cases, a total of 17 cases altogether. Remaining references are shown in *Table V*.

Table V.—CASES IN THE LITERATURE
(Additional to those in *Table IV*)

	Author	*No. of Cases*
Certain	Forbes and Duncan (1937)	2
	Lazarus and Marks (1943)	1
	Wilhelm (1944)	1
	Ewell and Jackson (1941)	1
	Barnes and Hill (1942)	1
	Forbes (1940)	1
	Abel (1953)	1
Probable	Lockhart-Mummery (1938)	1
	Craig and Lee Brown (1927)	1

Fistulæ in regional ileitis occur in three groups: (1) External to the anterior abdominal wall; (2) Internal; (3) Rectal and perirectal.

The cases in the first group occur exclusively after laparotomy and present commonly at the operation site, but occasionally track more distantly. Colp (1938) found 33 fistulæ following 2840 appendicectomies, an incidence of 1·1 per cent, whereas Clark and Dixon (1939) and Crohn (1949) found 45 external fistulæ in 342 cases of regional ileitis, an incidence of approximately 13 per cent. Internal fistulæ occurred in 23 of Crohn's 298 cases and in 2 of the 7 cases personally observed by me, whilst Pugh (1945) found 6 internal fistulæ in 17 cases of regional ileitis. The tracts originate in the sodden leaking ulcerated terminal ileum, usually on the side of the mesenteric attachment, and traverse the mesentery to terminate in an adjacent loop of small intestine, any segment of large intestine, or any adjacent hollow intra-abdominal viscus such as the ureter, bladder, Fallopian tubes, or uterus. The weighted diseased loop of ileum tends to droop into

the pelvic cavity and adhesions in this situation are common. This was clearly seen in a case of Crohn's disease of my own series, in which the terminal ileum was adherent posteriorly to the rectosigmoid and anteriorly to the bladder, representing a pathological phase through which the case initially described must have passed. The terminal ileum is the common primary site of fistula formation; in Brown and Donald's 178 cases of regional ileitis, all 8 of the internal fistulæ which were encountered originated in the terminal ileum or ileum and colon, and likewise 32 out of 33 of the external fistulæ (Crohn, 1949).

Analysis of the internal fistulæ in Crohn's (1949) series is shown in *Table VI*.

Thus in 23 cases of internal fistula the bladder is involved four times, that is in 17 per cent. Barium

Table VI.—INTERNAL FISTULÆ IN CROHN'S SERIES OF 298 CASES OF REGIONAL ILEITIS

Site of Fistula	*No.*
Ileum to sigmoid	6
Ileum to cæcum	3
Ileum to ascending colon	3
Ileum to ileum	5
Ileum to duodenum	2
Ileum to urinary bladder	4

follow-through radiographs may show fine lines emanating from the diseased ileum; these indicate potential fistulæ and are frequently seen overlying the dome of the urinary bladder. As in diverticulitis, then, urinary symptoms are not uncommon in regional ileitis even in the absence of vesical fistula.

Perirectal fistulæ originate either by infection of the crypts of Morgagni, from infected fæces, or by escape through the pelvic floor of proteolytic material from the porous loop of terminal ileum lying in the pelvis. The age and sex incidence of the cases of vesico-intestinal fistulæ due to regional ileitis are set out in *Table VII*.

Thus it is seen that the youngest case is 20 years of age and the oldest 51, the average being 30·4 years.

Table VII.—AGE AND SEX INCIDENCE OF VESICO-INTESTINAL FISTULÆ DUE TO REGIONAL ILEITIS

Author	*Age of Case*	*Sex*
Lockhart-Mummery (1938)	33	M.
Lazarus and Marks (1943)	24	M.
Wilhelm (1944)	32	M.
Forbes and Duncan (1937)	20, 36	M. and F.
Forbes (1940)	24	M.
Craig and Lee Brown (1927)	51	F.
Author	23	F.
Abel (1953)	—	F.

This is in marked contrast to the average age of the larger group of vesico-intestinal fistula, which is over 50 years. Furthermore, the number of females involved is proportionately higher in Crohn's disease, 5 males being affected and 4 females. In 282 cases of regional ileitis analysed by Crohn (1949), 162 occurred in males and 120 in females, so that males preponderate in the ratio of 4 males to 3 females. Thus the sex incidence of regional ileitis and the sex incidence of vesico-intestinal fistula due to regional ileitis are not widely disproportionate. This increased incidence of fistula in the female in regional ileitis is no doubt due to the facility with which the terminal ileum may adhere to the bladder, equally as well in women as in men.

Neoplasms.—Neoplastic fistulæ account for 64 of the present series, that is, 44 per cent, and inflammatory fistulæ for 51, or 32 per cent: there are 45 cases of neoplasm of the large intestine as compared with 26 cases of inflammation of the large intestine, the latter group composed of 23 cases of diverticulitis, 2 cases of tuberculous enterocolitis, and 1 case of actinomycosis. The cases of carcinoma of the sigmoid and rectosigmoid, numbering 24, are as common as those of diverticulitis. Rankin, Bargen, and Buie (1932) state that diverticulitis is responsible for 37 per cent of vesicocolic fistulæ, and carcinoma of the colon for only 17 per cent; in the present series, however, diverticulitis is responsible for no more cases than is carcinoma of the colon, and it is of interest to note that Rankin, during the discussion on Morrissey's paper (1931), stated that of his 26 personal cases of vesico-intestinal fistula 12 were due to diverticulitis and 10 to malignant disease, a comparative incidence more in keeping with the present findings. In this series, when carcinoma of the sigmoid and rectum are considered together, there is no doubt that carcinoma of the distal large intestine, responsible for 44 cases, is a commoner cause of fistula than is diverticulitis.

Whereas carcinoma of the right colon is commoner in the female, carcinoma of the left colon is commoner in the male, and carcinoma of the rectum is twice as common in men as in women (Dukes, 1946, 1947). Only 14 per cent of carcinomata of the large intestine occur in the cæcum, 29 per cent occur in the sigmoid, and 39 per cent in the rectum (Bailey and Love, 1952). In this series only 1 case of carcinoma of the cæcum is cited, in contrast to 44 cases of carcinoma of the sigmoid and rectum. This high incidence in the causation of fistula of malignant disease, which is so much commoner in the male, is partly responsible for the higher incidence of vesico-intestinal fistula in the male, but a factor of importance as a preventative circumstance in the female is the position of the vagina, uterus, and adnexa between the bladder on the one hand and the sigmoid and rectum on the other. That this barrier is circumvented in terminal ileal disease is seen by the relatively increased incidence in the female of vesico-intestinal fistula in cases of Crohn's disease.

There are 8 cases of neoplasms arising in sites exclusive to women—namely, 2 in the ovary, 5 in the cervix, and 1 in the vagina. The carcinomata of cervix and vagina cause fistula either by direct invasion of rectum and bladder or as a result of their treatment by radiotherapy, which in a number of cases is followed by necrosis of rectovaginal and vesicovaginal septa and a recto-vaginovesical communication in which urine and fæces are passed from the vagina.

Ten carcinomata causing fistulæ arose in the bladder and 1 in the prostate. Thus of 64 cases of malignant vesico-intestinal fistula, 11 arose from the urinary system, 8 from the female genital tract, and 45 from the alimentary tract, all these last arising from the large bowel.

Final Analysis of 115 Cases of Acquired Non-traumatic Fistula.—

1. Eighteen (15·6 per cent) arose from disease of the urinary tract, and 85 (73·9 per cent) from disease

of the alimentary canal. This, then, is the primary aetiological site in the great majority of cases.

2. Of the 85 cases of intestinal disease, 10 involved the small intestine; none of these latter cases are neoplastic, all are inflammatory.

3. Of the 85 cases of intestinal disease, in 71 the primary site is the large intestine; this then, is the primary site in 62 per cent of the above 115 cases.

4. Of the 71 cases of large-bowel involvement, 45 cases are of neoplastic disease; these constitute 39 per cent of the total of acquired non-traumatic vesico-intestinal fistulæ. Malignant disease of the large intestine is then likely to be a much more important factor in the causation of fistula than diverticulitis, which constitutes only 20 per cent of the cases.

5. Of the 18 cases of disease of the urinary tract, 7 are inflammatory and 11 neoplastic; that is, of urinary tract disease causing vesico-intestinal fistula, 61 per cent is malignant and 39 per cent inflammatory.

6. Of malignant disease of the urinary tract, carcinoma of the bladder occurred in 10 cases, but carcinoma of the prostate in only 1 case. It is important to note that some prostatectomies followed by fistula were for carcinoma.

7. Inflammatory disease of the uterine adnexa has not been encountered, although in the past numerous cases have been described, especially tuberculous salpingitis. It would seem that in the female genital tract, as in the urinary tract and in the alimentary tract, in each locality apart from the small intestine and appendix, neoplastic disease is of greater significance in fistula formation than is inflammatory disease. The 8 cases of malignant disease of the female genital tract constituted 7 per cent of the total 115 cases.

8. An analytical summary is given in *Table VIII*.

Table VIII.—Analytical Summary of 115 Acquired Non-traumatic Fistulæ

Primary Site	*Inflammatory Cases*	*Neoplastic Cases*
Alimentary tract	40	45
Urinary tract	7	11
Female genital tract	0	8
	47	64

PATHOLOGY

Fistulæ are usually single, involving two or three organs, but they may be multiple, as noted by Wilhelm (1944) and also Duff (1937). In *Table IX* is given the frequency of fistulæ in the various sites encountered in 131 cases.

Table IX.—Site Incidence in 131 Cases of Fistulæ

Type of Fistula	*No.*
Ileovesical	9
Cæcovesical	2
Appendicovesical	3
Colovesical	8
Sigmoidvesical	38
Rectovesical	65
Recto-vesico-ileal	1
Recto-ileo-vesical	1
Recto-vagino-vesical	3
Vesico-recto-urethral	1

The communications found are of three types: direct, tracts, and cavities. Direct communications occur usually in malignant disease and sometimes in tuberculosis; other instances are simple appendico-vesical fistulæ and, rarely, the vesicosigmoid fistula constituted by a single, long diverticulum adherent directly to the bladder. Tracts are usually found in fistulæ of inflammatory origin; they are long, tortuous, and lined by granulation tissues. Cavities originate as perivesical abscesses due to perforation of inflammatory or neoplastic visceral lesions, the abscesses in their turn rupturing into the bladder; many of these cavities contract down subsequently to form tracts, but some persist as in the so-called appendico-pyovesical fistulæ, and in some cases complicating diverticulitis.

In general, communications due to inflammatory disease and trauma are small and those due to malignant disease are large.

Fistulæ from an extravesical source may open into the bladder in one of three situations—namely, just above the trigone, in the vault, and on the anterior wall. Higgins (1936), analysing 122 cases, found that the first site was by far the commonest. Ileovesical, cæcovesical, and appendicovesical fistulæ tend to open on the right side and the vesicosigmoid type on the left. The bladder prior to the formation of a fistula from an extravesical source usually shows at the incipient site a localized area of cystitis or bullous œdema; the latter, if gross, presents a pseudopolypoid appearance. The orifice of an established fistula may present in the base of a necrotic ulcer or in an area of exuberant granulation tissue, or it may be lost in an area of gross cystitis; occasionally in long-standing cases it is surrounded by a zone of fibrosis and is clearly defined. In malignant cases the orifice is usually concealed by surrounding necrotic new growth. The bladder itself, with the establishment of a fistula, generally shows an acute generalized cystitis, but occasionally there is surprisingly little change. Chronic cystitis usually supervenes and the bladder ultimately becomes contracted and fibrotic. It is noteworthy that only in a minority of cases does acute ascending pyelonephritis occur in the early stages (Mayo and Miller, 1940). With the supervention of fibrous contracture of the bladder ureteric obstruction results, and the usual sequelæ—hydro-ureter, hydronephrosis, infection, and renal failure—follow. In Parham and Humes' series (1909) of 25 cases which came to autopsy, pyelitis was present in 18 and was bilateral in 15. There are, of course, cases on record in which patients with vesico-intestinal fistula have survived for as long as forty years (Duff, 1937). Involvement of other viscera by the inflammatory or neoplastic process is common, and may be widespread around the fistula, affecting the alimentary tract at other levels, the uterus, tubes, ovaries, vagina, omentum, and abdominal parietes.

CLINICAL FEATURES

The clinical picture presented by vesico-intestinal fistula may be considered to show three phases: the first is the stage of the clinical syndrome of the causative lesion; the second is the stage of incipient fistula; and the third is the stage of established fistula.

The first phase is, of course, variable in its manifestations. Thus the patient with ileitis or

appendicitis suffers recurrent pain in the right iliac fossa, with sigmoid diverticulitis there is pain in the left iliac fossa, carcinoma of the rectum causes rectal bleeding or altered bowel habit, and the patient with carcinoma of the bladder usually has hæmaturia. Uterine and cervical carcinoma are associated with vaginal bleeding and discharge.

The second phase usually follows insidiously—the stage of incipient fistula when the cardinal manifestations are frequently of micturition and the passage of cloudy urine containing albumin.

Finally, stage three supervenes when the fistula is established. The onset is in one of two ways: the first, the commoner, is insidious, with increased frequency of and burning pain on micturition, deterioration in the general condition, wasting, and mental depression; the second, uncommon, is 'explosive', with sudden extreme frequency, strangury, rigors, loin pain, vomiting, and fever betokening an acute ascending pyelonephritis. In none of my own personal series did this occur. There are two manifestations which indicate unequivocally the the presence of a vesico-intestinal fistula: they are the passage of fæces in the urine and the passage of urine from the rectum. The former is commoner in general, although again in my small series urine was passed from the rectum in three instances (*Cases* 4, 6, and 7). The determining factor seems to be the site of the fistula in the bladder; thus a high vesical fistula as occurs in the vesicosigmoid type is usually associated with fæcal contamination of the urine, but a low bladder fistula opening on the trigone, as occurs in carcinoma of the bladder and carcinoma of the rectum, is not infrequently associated with the voiding of urine from the rectum.

Pneumaturia occurs with great frequency, but is not pathognomonic. It is experienced usually at the end of the act of micturition, and in non-fistulous cases may be due to one of three conditions—firstly, the introduction into the bladder by instrumentation of air; secondly, fermentation of diabetic urine; or, thirdly, infection of the urine by certain organisms, *Escherichia coli*, *Aerobacter aerogenes*, or *Coccobacillus vesicæ*, all of which acidify the urine and cause bicarbonate breakdown with evolution of carbon dioxide. The onset of fistula is particularly difficult to detect in cases of carcinoma of the bladder where so frequently cystitis is present beforehand. In general it may be said that the coexistence of bladder and bowel symptoms is very suggestive.

DIAGNOSIS

This depends on the usual quartet of clinical investigations—namely, history, external examination, internal examination, and special examinations. There may be a history of abdominal pain, change of bowel habit, especially diarrhœa, urinary disorders, urinary disorders associated with disorders of bowel action, and rectal or vaginal bleeding. Few patients complain of passing urine from the back passage. Loss of weight is usual.

On external examination the patient's general condition is often poor, but occasionally it is surprisingly good. External fistulæ may be found on abdomen or perineum; urine may be seen leaking from the rectum or emission of gas from or fæcal staining of the urethra observed. A mass may be palpable per abdomen, but in general this is found only in a minority.

Internal digital examination of the pelvis may reveal a mass in the rectum, prostate, bladder, vagina, cervix, uterus, uterine adnexa, or pouch of Douglas, but except in very large rectovesical or rectovaginovesical fistulæ it is unusual to feel the actual fistulous communication.

Special investigations are of particular importance. Urine analysis in the stage of incipient fistula reveals albumin in vesical specimens, whereas those gained by ureteric catheterization are quite clear. Subsequently with establishment of a fistula, fæcal particles may be detected microscopically—namely, fragments of undigested muscle and starch. A positive finding is proof of the existence of a vesico-intestinal fistula. Examination of the fæces for urine is important also; Dukes (1938) considers the best method to be by urea estimation.

On proctosigmoidoscopy the fistula, even when theoretically accessible, is usually invisible because of the presence of marked œdema around the opening and also frequently of a mass which prevents manipulation of the sigmoidoscope. Urine, however, may be seen in the rectum, and if at the time boric lotion containing methylene blue is introduced into the bladder, some may be seen emerging from the site of the fistula.

At cystoscopy the findings coincide with the pathological picture of the bladder described above; again the fistula is often invisible because of gross cystitis, œdema, bleeding, or fungating new growth. The fistula was seen in two of the small personal series observed: one was the traumatic fistula in *Case* 3, and the other was the urethral opening of the vesico-recto-urethral fistula found in *Case* 7. Barnes and Hill (1942), reporting a series of 14 cystoscopies on cases of vesico-intestinal fistula, saw changes in the bladder in 13 but the actual fistula in only 2 cases. Fæces or gas may be seen emerging from the vesical aperture or this may be revealed by observing the bladder with a cystoscope whilst methylene blue in boric lotion is introduced into the rectum. Carcinoma of the cervix and fistulæ involving the vagina are seen through a speculum. Barium follow-through or enema may show the causative intestinal lesion, but not usually the fistula, which is generally small and not filled.

A cystogram is often more successful than barium enema in revealing the fistula.

Charcoal given by mouth is quickly voided in the urine when an ileovesical fistula is present.

Biopsy, of course, is of considerable importance in diagnosis and in planning treatment. Attempts should always be made to obtain sections of the fistula through cystoscope, sigmoidoscope, or vaginal speculum.

Ultimate diagnosis, as in the case of Crohn's disease with vesico-ileorectal fistula described initially, may depend finally on laparotomy.

Ancillary investigations of great value are full blood-count, plasma-protein analysis, intravenous pyelography, blood-urea, estimation, W.R., and radiographs of the chest.

PROGNOSIS

This depends on the cause, on the age and general condition, and on the presence or absence of complications. Spontaneous recovery seems to occur only in the traumatic type. Pascal (1899) estimated the average duration of life as three years.

TREATMENT

The treatment of vesico-intestinal fistula depends essentially on the cause, the condition of the patient, and any complications.

In general, treatment in the acute phase consists of diversion of the urinary stream and antibiotic therapy, and that in the chronic phase comprises diversion of the urinary and fæcal streams and surgical repair.

Congenital fistulæ are isolated, ligated, and divided in conjunction with operations to establish a perineal anus, with or without a preliminary colostomy. Where a considerable interval separates the rectal stump from the perineum, ligation and division of the fistula is an essential step in mobilizing the rectum, and the dissection is probably best carried out from above. In two cases personally encountered, one with a fistula and one without, in which the rectal stump was high, it could certainly be neither adequately nor accurately mobilized from the perineum.

Traumatic fistulæ are probably the only type where spontaneous healing may occur. In the accident or wounding cases the immediate necessity is treatment of shock and initiation of antibiotic therapy. As soon as the patient's condition permits, exploratory laparotomy should be performed to exclude intraperitoneal injury or leak. Most of these fistulæ are rectovesical, and it has been observed that whereas those due to accidents or wounding heal without great difficulty, those following surgical trauma do not do so. The large accidental fistula may be attacked by the transvesical route and repaired in layers; the post-operative fistula is approached by the transvesical or perineal route. When the accidental fistula is small, as it usually is, suprapubic or perurethral drainage of the bladder and the initiation of intestinal chemotherapy commonly suffice; when the fistula is large, however, it is a wise precaution to divert the fæcal stream by means of a colostomy, and if this is done early it may obviate the necessity for direct attack upon the fistula.

The fistula formed by Meckel's diverticulum, the appendix, or a single sigmoid diverticulum is readily cured by appendicectomy or diverticulectomy and closure of the opening in the bladder, followed by temporary vesical drainage.

In the treatment of vesicosigmoid fistula due to diverticulitis it is now generally agreed that the initial step must be the establishment of a proximal colostomy to divert the fæcal stream. This may suffice to heal the fistula, but continuity of the colon should not be restored for at least twelve months; if there is some colon obstruction present, preliminary colostomy results in subsidence of the pericolitis and makes resection of the affected segment of sigmoid much easier at a later date.

The management of vesico-intestinal fistula complicating tuberculous cystitis is a very difficult problem. Fistula formation is commonly almost terminal. In acute cases, when discomfort is severe and the general condition deteriorating rapidly, suprapubic cystotomy may afford considerable relief and amelioration. Subsequently, if the disease appears to be unilateral nephro-ureterectomy on that side may be performed. In bilateral cases reliance must be placed on antibiotic treatment with or without chemotherapy. In cases occurring in association with fibrous contracted bladder, if an intravenous pyelogram shows bilateral grossly dilated ureters nothing is to be gained by surgical intervention; if, however, the ureters are not grossly dilated and the renal function is good, then bilateral ureteric transplantation to circumvent later ureteric obstruction should be performed; if unilateral renal disease is present then nephro-ureterectomy should be carried out.

In cases of vesico-intestinal fistula due to tuberculous enteritis and Crohn's disease the objects of treatment are direct attack on the fistula and ablation of the diseased segments of the intestine. Permanent short-circuiting operations have no place in the treatment of vesico-intestinal fistula due to regional ileitis. The diseased segments of intestine must be resected, although, of course, such a procedure may be carried out in stages. Below are the salient features of 5 cases of particular interest:—

Lockhart-Mummery's Case (1938).—
A man of 33 who had a recto-ileovesical fistula: colostomy proximal to the fistulous opening into the rectum had been performed: he not only passed fæces in his urine but also passed urine and fæces through both barrels of his colostomy. This condition had remained for several years: he was cured by resection of the last foot of terminal ileum, cæcum, and ascending colon, with closure of the apertures in bladder and rectum. The colostomy was closed subsequently.

Forbes and Duncan's Case (1937).—
A man of 20 with an ileovesical fistula due to Crohn's disease. In the first place a short-circuiting ileotransverse colostomy was performed, with some improvement in the general condition for one month. Symptoms then became more severe than ever and at a second operation the ileum beyond the ileotransverse anastomosis was closed and ileostomy of the distal loop performed. The general condition again improved, but Crohn, discussing the case later, stated that subsequently a very severe recurrence of ileitis occurred.

Forbes' Case (1940).—
A woman of 36 who had regional ileitis: a short-circuiting ileotransverse colostomy was performed. Despite this, after six years she developed an ileovesical fistula from the diseased loop. The fistula was divided and the openings in the bladder and terminal ileum closed. A fæcal fistula developed immediately and took three months to close.

Wilhelm's Case (1944).—
A man of 32 had a rectovesico-ileal fistula. The ileum was separated from the bladder and after closure of the ileal and vesical apertures ileotransverse colostomy was performed followed by suprapubic cystotomy and left inguinal colostomy. Four weeks later the distal loop of ileum, the diseased segment, was excluded. After four months the left inguinal colostomy was closed: sixteen days later pneumaturia recurred and transverse colostomy was established. Eighteen months later effervescent blue solution introduced into the rectum

appeared in the urine and it was obvious that a direct attack on the residual rectovesical fistula would have to be made.

Pugh's Case (1945).—
A patient with regional ileitis involving both the terminal ileum and sigmoid (the 'ileocolitis' of Crohn's classification) developed an ileosigmoidovesical fistula. The involved ileum was resected, the bladder fistula closed, and a temporary single-barrel ileostomy fashioned: the affected segment of sigmoid was ablated by the Mikulicz exteriorization procedure and a double-barrel colostomy established. Continuity of the sigmoid was subsequently restored and at a third stage the ileostomy was dismantled and ascending ileocolostomy performed.

From a study of these cases it is observed that in Crohn's disease:—

1. Short-circuiting of a diseased segment of intestine does not prevent the formation of a fistula.
2. Short-circuiting does not heal an established fistula.
3. Cure is gained only by direct attack on the fistula and ablation of the affected loops of intestine.

Pre-operative correction of dehydration, blood transfusion, and intestinal chemotherapy are essential procedures. If the diseased loops of the gut are resectable, nothing is to be gained by delaying ablation, but if adhesions make this a hazardous or protracted procedure then a preliminary short-circuit with exclusion may improve the situation and facilitate subsequent radical operation.

The treatment of neoplastic vesico-intestinal fistula has in recent years undergone much change; many cases previously considered inoperable are now subjected to radical surgery. Factors responsible for the change are careful pre-operative preparation, with attention especially to the nutritional state and intestinal antisepsis, and the concept of pelvic evisceration with ureteric transplantation into isolated loops of gut, so avoiding the misery of the 'wet colostomy'.

SUMMARY

Seven cases of vesico-intestinal fistula, including one due to Crohn's disease, were encountered. These, together with 141 cases gathered from the personal series of all types experienced by fifteen other surgeons, make a total of 148, which are analysed from the point of view of aetiology.

Seventeen cases of vesico-intestinal fistula due to regional ileitis have been gathered together.

The importance of neoplasm in the production of fistula is stressed; it is twice as common an aetiological factor in the production of the fistulæ between the bladder and distal large intestine as is diverticulitis. The significance of Crohn's disease in the production of vesico-intestinal fistula in women is noted.

Pathology, clinical features, diagnosis, and treatment are reviewed. The importance of resection of the involved segments of intestines in cases due to regional ileitis is stressed.

It is a privilege to record my indebtedness and gratitude to those under whose guidance I have worked—namely, Mr. D. Ioan-Jones, Mr. R. A. Mogg, and Mr. Melbourne Thomas—and by whose kind permission I am able to publish details of the personally encountered and treated cases; also to Professor Lambert Rogers for his helpful criticism, advice, and encouragement.

REFERENCES

ABEL, A. L. (1953), personal communication.
ALBANO, G. (1926), *Arch. ital. Chir.*, **16**, 133.
BAILEY, H., and MCNEIL LOVE, R. J. (1952), *A Short Practice of Surgery*. London: Lewis.
BALCH, J. F. (1936), *J. Urol.*, **36**, 706.
BARNES, R. W., and HILL, M. R. (1942), *Calif. West. Med.*, **56**, 350.
BRYAN, R. C. (1916), *Ann. Surg.*, **63**, 353.
CLARK, R. L., jun., and DIXON, C. F. (1939), *Surgery*, **5**, 277.
COLP, R. (1938), *Ann. Surg.*, **107**, 74.
CRAIG, R. G., and LEE BROWN, R. K. (1927), *Surg., Gynec. Obstet.*, **44**, 753.
CRIPPS, H. (1888), *The Passage of Air and Fæces from the Urethra*. London: Churchill.
CROHN, B. B. (1949), *Regional Ileitis*. New York: Grune and Stratton.
— — GINZBERG, L., and OPPENHEIMER, G. D. (1932), *J. Amer. med. Ass.*, **99**, 1323.
DUFF, A. (1937), *Brit. J. Surg.*, **25**, 466.
DUKES, C. (1938), *Proc. R. Soc. Med.*, **31**, 1281.
— — (1946), *Ibid.*, **38**, 381.
— — (1947), *Ibid.*, **39**, 763.
EWELL, G. H., and JACKSON, R. H. (1941), *J. Urol.*, **46**, 693.
FORBES, R. D. (1940), *Northw. Med., Seattle*, **39**, 174.
— — and DUNCAN, J. (1937), *West. J. Surg.*, **45**, 362.
HIGGINS, C. C. (1936), *J. Urol.*, **36**, 694.
KELLOGG, W. A. (1938), *Amer. J. Surg.*, **41**, 135.
LADD, W. E., and GROSS, R. E. (1948), *Abdominal Surgery of Infancy and Childhood*. Philadelphia: W. B. Saunders.
LANGE, J. (1949), *Nord. med.*, **42**, 1612.
LAZARUS, J. A., and MARKS, M. S. (1943), *Amer. J. Surg.*, **59**, 526.
LOCKHART-MUMMERY, J. P. (1938), *Proc. R. Soc. Med.*, **31**, 1281.
MAYFIELD, L. H., and WAUGH, J. M. (1949), *Ann. Surg.*, **130**, 186.
MAYO, C. W., and MILLER, J. M. (1940), *Arch. Surg., Chicago*, **40**, 897.
MORRISSEY, J. H. (1931), *J. Amer. med. Ass.*, **96**, 843.
NORBURY, L. E. C. (1938), *Proc. R. Soc. Med.*, **31**, 1281.
ORMOND, J. K., BEST, J. W., and KLINGER, M. E. (1949), *Surg. Gynec. Obstet.*, **89**, 411.
PARHAM, F., and HUME, J. (1909) *Ann. Surg.*, **50**, 251.
PASCAL, A. (1899), "Des fistules vesico-intestinales acquises chez l'homme et la femme", *Thèse de Paris*.
PEMBERTON, J., POOLE, T. L., and MILLER, J. M. (1940), *J. Urol.*, **44**, 274.
PUGH, H. L. (1945), *Ann. Surg.*, **122**, 845.
RANKIN, F. W., BARGEN, J. A., and BUIE, L. A. (1932), *The Colon, Rectum and Anus*. Philadelphia: W. B. Saunders.
— — and BROWN, P. W. (1930), *Surg. Gynec. Obstet.*, **50**, 836.
REBORI, F. (1944), *Semana. Med.*, **1**, 177.
ROBINSON, J. N., CULP, O. S., SUBY, H. I., REISER, C. W., and MULLENIX, R. B., (1946), *J. Urol.*, **56**, 498.
SPRIGGS, E. (1927), *Proc. R. Soc. Med.*, **20**, 57.
SUTTON, G. D. (1921), *Surg., Gynec. Obstet.*, **32**, 318.
TELLING, M. W. H., and GRUNER, O. C. (1916), *Brit. J. Surg.*, **4**, 468.
WILHELM, S. F. (1944), *Surg. Gynec. Obstet.*, **79**, 427.
WILLAN, R. J. (1933), *Brit. med. J.*, **2**, 140.

RECURRENT PYOGENIC CHOLANGEITIS

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INTRODUCTION

In a paper entitled " Common-duct Stones of Liver Origin ", Digby (1930) drew attention to the occurrence in Hong Kong of some aspects of the syndrome which is the subject of this communication. In this paper he described 8 cases, and in a further communication (Digby, 1934) he added an additional 7 cases. In comparing the clinical picture of stones in the biliary tree in patients of European stock with that encountered in Chinese in Hong Kong, he stated : " In Chinese patients, as seen in Hong Kong, we find an entirely different clinical picture (from that encountered in European stock). Stones in the common duct usually originate in the liver. When they reach the common duct they grow to a remarkable size and lead to a distension of the gall-bladder, thus breaking Courvoisier's law. They produce a striking and unmistakable syndrome." This syndrome he described as consisting of attacks of pain in the epigastrium and right hypochondrium accompanied by some degree of jaundice and by fever associated with rigors, and on examination the liver and gall-bladder were greatly enlarged. These symptoms and signs were regarded by him as pathognomonic of intrahepatic stone formation with impaction of stones in the common duct.

Early in the course of our clinical and pathological experience in Hong Kong it became evident that common-duct stones were frequently not strictly of liver origin as Digby believed, and that the clinical syndrome described by him occurred commonly in the absence of cholelithiasis. Indeed, the condition could progress to a fatal termination without the occurrence of gall-stones. These observations led us to investigate the problem, and the purpose of this paper is to report the results of our investigations.

MATERIAL

The clinical material on which this study is based consists of 90 consecutive patients suffering from recurrent pyogenic cholangeitis admitted to our wards in the Queen Mary Hospital in the years 1950 to 1952. The material on which the pathological study was made consists of biopsy specimens obtained from the clinical series and all cases of calculi in the intrahepatic and extrahepatic biliary tree, together with all cases of pyogenic cholangeitis occurring in the absence of organic obstruction to the biliary tree coming to autopsy in the years 1949 to 1952. All the patients were Chinese.

Table I.—Analysis of Material in Groups 1 and 3 according to the Distribution of Calculi

Group	Distribution of Calculi	No. of Cases	
Group 1	Patients submitted to laparotomy	66	
1-A	Confined to gall-bladder	20	
1-B	Present in gall-bladder and biliary tree	7	
	1. Present in gall-bladder and common bile-duct		6
	2. Present in gall-bladder and intrahepatic ducts		1
1-C	Confined to the biliary tree	25	
	1. Confined to the common bile-duct		15
	2. Present in common bile-duct and intrahepatic ducts		5
	3. Confined to intrahepatic ducts		5
1-D	No calculi demonstrated	14	
Group 3	Autopsy material	20	
3-A	Present in gall-bladder, common bile-duct, and intrahepatic ducts	3	
3-B	Confined to the biliary tree	14	
	1. Confined to the common bile-duct		3
	2. Present in common bile-duct and intrahepatic ducts		2
	3. Confined to the intrahepatic ducts		9
3-C	No stones demonstrated	3	

The material is conveniently divided into three groups. Group 1 consists of 66 cases in which laparotomy was performed. Group 2 consists of those cases in which laparotomy was not performed, but in which the clinical, laboratory, and pathological findings were consistent with a diagnosis of recurrent pyogenic cholangeitis. In 21 of the 24 cases of this group laparotomy was considered unwarranted, and in the remaining 3 cases operation was refused. Group 3 consists of the autopsy material. Groups 1 and 3 are further divided into subgroups according to whether stones were present or absent and, when present, according to their distribution. The details in both these groups are set out in *Table I*. The presence of stones and their distribution was determined by cholecystography, by palpation, and instrumental exploration at laparotomy, and by post-operative cholangiography of both the intrahepatic and extrahepatic biliary tree.

It should be noted, however, that from our observations at autopsy we consider that cholangiography will fail to demonstrate certain intrahepatic stones, especially when these lie in the periphery of the liver.

SEX INCIDENCE

The sex incidence in the 110 cases of all three groups is set out in *Table II*, from which it will be seen that 62 (56·4 per cent) were males and 48 (43·6 per cent) were females. Of the 69 cases of Groups 1 and 3 in which calculi were demonstrated, 37 (53·6 per cent) were males and 32 (46·4 per cent) females. The sex incidence was equal in the 30 cases in Groups 1 and 3 in which calculi were present in the gall-bladder. This equal sex incidence is at variance with that reported in European stock. American and European writers agree on the predominance of cholelithiasis in women. Littler and Ellis (1952) reported a ratio of females to males of almost 5 to 1, Adams and Stranahan (1947) 3 to 1, and Marshall and Phillips (1948) and Robertson (1945) 2 to 1. Miyake and Ishiyama (1930), however, reported an almost equal sex incidence in Japan, and it is of interest to note that Rufanov (1936), in an analysis of cases of intrahepatic stone reported in the literature up to that time, found an equal sex incidence.

Table II.— Sex Incidence

Group	Sex	
	Male	Female
Group 1	34	32
1-A	11	9
1-B	3	4
1-C	12	13
1-D	8	6
Group 2	15	9
Group 3	13	7
3-A	1	2
3-B	10	4
3-C	2	1
Total (all groups)	62	48

AGE INCIDENCE

The age incidence in decades on admission to hospital or at autopsy is set out in *Table III*. This table also shows the age incidence at the onset of symptoms in Groups 1 and 2. It will be seen that the peak incidence in Group 1 occurred in the third, fourth, and fifth decades. This peak incidence holds for the subgroups 1-A, 1-B, and 1-C, but in 1-D it shifts to the second, third, and fourth decades. If all cases in Group 1 are considered, more occurred in the second decade than in the sixth, seventh, and eighth decades combined. This incidence differs from that encountered in European stock. Although it is recognized that gall-stones may occur at any age, American and European writers agree that after the age of 40 the incidence rises rapidly (Dessau, 1943; Robertson, 1945; Littler and Ellis, 1952). Further, 38 per cent of the cases reported by Marshall and Phillips (1948) and 27 per cent of those reported by Littler and Ellis (1952) were 60 or over, whereas of the cases with cholelithiasis in Group 1 less than 6 per cent were over this age. *Fig.* 215 contrasts graphically the incidence by decades of all cases of cholelithiasis in Group 1 with that reported by Littler and Ellis (1952), and shows clearly that in the Chinese in Hong Kong gall-stones form in younger age groups.

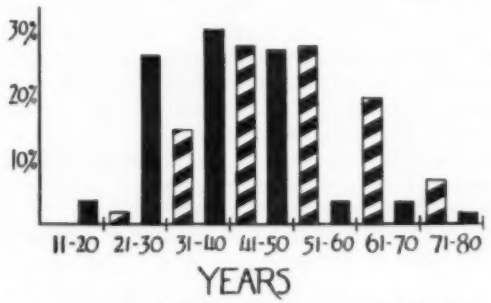


Fig. 215.—Age incidence of cases of cholelithiasis in the present series (black line) compared with that of the series reported by Littler and Ellis (1952).

Table III.—Age Incidence in Decades at Onset of Symptoms and on Admission to Hospital in Groups 1 and 2. Age Incidence at Autopsy in Group 3

Group	No. of Cases	Age on Admission to Hospital or at Autopsy								Age at Onset of Symptoms							
		Decade								Decade							
		1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
Group 1	66	—	7	19	19	16	2	2	1	6	19	19	13	4	3	1	1
1-A	20	—	—	5	7	5	2	—	1	—	1	9	5	2	2	—	1
1-B	7	—	—	1	1	3	—	2	—	—	—	2	3	—	1	1	—
1-C	25	—	2	8	8	7	—	—	—	2	12	4	5	2	—	—	—
1-D	14	—	5	5	3	1	—	—	—	4	6	4	—	—	—	—	—
Group 2	24	2	9	10	3	—	—	—	—	7	11	6	—	—	—	—	—
Group 3	20	—	3	3	7	4	2	1	1								
3-A	3	—	—	—	2	—	—	1	—								
3-B	12	—	1	2	4	3	1	—	1								
3-C	6	—	2	1	1	1	—	—	—								
Total (all groups)	110	2	19	32	29	20	4	3	2	13	30	25	13	4	3	1	1

The average age at operation of cases with stones in the gall-bladder was 40·6 years. This is not significantly different from that reported in European stock, for example, in the series reported by Bockus, Willard, and Metzger (1935) it was 42 years. A significant difference emerges when the average age of cases with stones in the common bile-duct is considered. Judd and Marshall (1931) analysed 1768 cases with stones in the common bile-duct and found that, while no age appeared exempt, the majority occurred in the fifth and sixth decades, and in a substantial number the condition made its first appearance in aged individuals. Glenn (1947) reported the average age of 124 cases with stones in the common bile-duct as 52 years. The average age in the present series was 33 years.

Table III shows the age incidence of the onset of symptoms in Groups 1 and 2. We have been unable to find in the literature an analysis of the age at onset of symptoms in European stock, but such information as has been obtained indicates that symptoms start in much younger age groups among the Chinese in Hong Kong.

Table IV.—Analysis of the Histories obtained in Groups 1 and 2

Group	No. of Cases	Pain		Fever		Jaundice	
		Previous Attacks	First Attack	Previous Attacks	First Attack	Previous Attacks	First Attack
Group 1	66	56	9	53	10	50	10
1-A	20	18	1	14	3	14	1
1-B	7	6	1	6	1	7	—
1-C	25	21	4	23	2	19	4
1-D	14	11	3	10	4	9	5
Group 2	24	14	5	16	8	11	13

CLINICAL HISTORY

The three dominant symptoms were those described by Digby (1930, 1934)—namely, attacks of fever, pain, and jaundice. The incidence of these symptoms in cases of Groups 1 and 2 are set out in *Table IV*. From this table it will be seen that in Group 1, 85 per cent had a previous history of recurrent attacks of pain, 14 per cent were admitted with the first attack. One case, in Group 1-A, had had no pain. In Group 2, 57 per cent had previous history of recurrent attacks of pain, 21 per cent were admitted in the first attack, and 5 cases had no such history.

Again from *Table IV* it will be seen that 80 per cent of Group 1 cases had a previous history of recurrent attacks of fever, 15 per cent were admitted in the first attack, and no fever occurred in the remaining 3 cases which all belonged to Group 1-A. In Group 2, 67 per cent gave a history of previous attacks of fever and the remaining 33 per cent were admitted in the first attack.

A previous history of jaundice was given by 76 per cent of cases in Group 1 and 46 per cent of cases in Group 2. In the majority of these cases there had been repeated attacks. In Group 1, 15 per cent were admitted with their first attack of jaundice, whereas in Group 2, 54 per cent of cases were admitted with their first attack. Jaundice had not occurred in 6 cases (9 per cent) in Group 1. In Group 1-A, in which stones were confined to the gall-bladder, jaundice occurred in 15 cases (75 per cent) and in 14 there was a history of previous repeated attacks. No jaundice had occurred in 2 cases in Group 1-C in which calculi were present in the common bile-duct.

The pain was most commonly of severe lancinating character of sudden onset, situated in the right hypochondrium or epigastrium, and frequently associated with vomiting. Colic was less common, and although occasionally occurring alone it was usually associated with the lancinating pain. Radiation of pain across the upper abdomen and through to the back was frequent, but radiation to the shoulder was rarely described. The duration and severity of individual attacks of pain varied widely, not only from case to case but from time to time in the same case.

The inhalation of amyl nitrite usually resulted in substantial but transient relief of pain; the subcutaneous injection of atropine ($\frac{1}{100}$ gr.) was less effective, but the relief afforded persisted for a longer period. It should be noted here that the lancinating pain occurred during post-operative cholangiography on two occasions, apparently as a result of rapid distension of the biliary tree associated with obstruction at the lower end of the common duct. When, later in the examination, the obstruction was overcome, some of the contrast medium passed into the duodenum and the pain immediately subsided.

The attacks of fever ranged from a low irregular pyrexia to high fever with repeated rigors, and the duration of individual attacks varied from a few days to many weeks. In the majority of instances no medical advice had been sought and the fever resolved spontaneously.

While pain and fever frequently coexisted, one could occur without the other. Again, pain might anticipate the onset of fever or follow it. The majority of patients described the stools as becoming pale following upon the more severe attacks of pain and fever. Many of the patients denied that there was coincidental jaundice, but most of these described the urine as being dark.

Jaundice rarely occurred without preceding attacks of fever and pain. It might appear with the first attack of fever or might not appear until repeated attacks had occurred over a period of years.

Usually, but not invariably, once jaundice had occurred it recurred with each subsequent attack. The jaundice was usually mild to moderate in intensity and on only three occasions was deep jaundice encountered. This was noted in one member each of Groups 1-A, 1-C, and 1-D. The duration of attacks varied very widely from a transient jaundice to one persisting for a period of years. The intensity fluctuated with recurrence of attacks of fever and pain in the cases with persistent jaundice. One case, which was seen before this investigation commenced and not included in the present series, was of a woman, aged 44, with stones confined to the gall-bladder who had had a fluctuating jaundice for eight years.

The following brief summaries illustrate the similarity of the histories encountered in recurrent pyogenic cholangeitis independent of the presence or absence of stones or their distribution. They illustrate also the wide variation in the incidence and severity of attacks and the variable relationship of pain and fever to the onset of jaundice.

A 10-year-old boy in Group 1-D since the age of 2 years had a history of six or more attacks of fever yearly, occasionally with rigors, and pain. Each attack was associated with jaundice, which was transient.

A 25-year-old woman in Group 1-A had a history for 2½ years of four or more attacks of fever each year, occasionally with rigors and pain. Each attack was associated with jaundice, which was transient.

A 14-year-old girl in Group 1-D had her first attack of fever with rigors and pain at the age of 12, when she became jaundiced. The jaundice persisted after other symptoms had disappeared, and over the subsequent period of two years it waxed and waned in intensity, the waxing coinciding with further attacks of fever and pain.

A 24-year-old man in Group 1-C had repeated attacks of pain and fever with rigors since the age of 4 years. In the first eleven years there was no jaundice, but in the last nine years jaundice occurred with each attack.

A 48-year-old man in Group 1-A commenced to suffer from attacks of fever and pain occasionally associated with jaundice some twenty-five years before admission. These attacks recurred at frequent intervals for four years, but he was free from attacks in the succeeding period of six years. The attacks recurred for one year and there followed a period of freedom for twelve years. In the three years before admission the attacks recurred, became more severe, and the jaundice became persistent.

Three patients, one each in Groups 1-A, 1-C, and 1-D, with a history of previous attacks of pyogenic cholangeitis, were first seen during an attack which was complicated by acute pancreatitis.

CLINICAL FINDINGS

The relevant clinical findings in Groups 1 and 2 are set out in *Table V*. It will be seen that 70 per cent of the cases in Group 1 had jaundice on admission and 50 per cent were in an acute febrile exacerbation of the disease. There was coincident jaundice in 29 of the 34 cases with fever. All 24 cases in Group 2 had jaundice on admission, and 15 of these were febrile at that time.

Table V.—Analysis of the Findings on Examination

Group	No. of Cases	Jaundice	Pyrexia	Abdominal Examination			
				No. of Cases with Adequate Assessment	Enlarged Liver	Palpable Gall-bladder	Enlarged Spleen
Group 1	66	46	34	53	36	20	11
1-A	20	10	10	13	7	6	3
1-B	7	5	4	6	4	3	1
1-C	25	20	14	22	15	6	4
1-D	14	11	6	12	10	5	3
Group 2	24	24	15	20	18	4	2

Examination was hampered by upper abdominal rigidity and tenderness in 13 of the 66 cases in Group 1. In 36 of the remaining 53 cases the liver was enlarged, the lower margin being defined 2–10 cm. below the costal margin in the midclavicular line. In 22 of the 36 cases with liver enlargement the gall-bladder was palpably enlarged and tender. In Group 2, 20 of the 24 cases could be adequately examined, and in 18 of these there was palpable tender enlargement of the liver. In 4 of the 18 cases the gall-bladder was palpably enlarged and tender.

The spleen was enlarged in 11 of the cases in Group 1 and in 2 of the cases in Group 2. In no case was the lower border more than 3 cm. below the costal margin. It should be noted that in the 13 cases with enlargement of the spleen biopsy of the liver showed a picture of established biliary cirrhosis.

Fifteen of the cases showed clubbing of the fingers and toes, and 11 of these had established biliary cirrhosis.

LABORATORY FINDINGS

The ranges of serum-bilirubin, alkaline phosphatase, and leucocyte counts in cases from both Groups 1 and 2 are set out in *Table VI*. It will be seen that the average bilirubin concentration of 3·4 mg. per cent agrees with the clinical assessment of the jaundice being mild to moderate in intensity. The alkaline phosphatase in jaundiced patients was unduly high when considered in relation to the degree of jaundice, the average in apyrexial jaundiced

cases being 27 K.A. units and in pyrexial jaundiced cases 42 K.A. units. It should be noted that in patients with fever in the absence of jaundice the alkaline phosphatase was also raised, the average being 30 K.A. units. All the pyrexial cases showed a leucocytosis ranging from 10,500 to 29,200 per c.mm. The differential count showed in the main a dominance of polymorphonuclear leucocytes, the average being 87 per cent.

The excretion of urobilinogen in the urine was increased not only in those cases showing jaundice but also in 40 per cent of the non-jaundiced cases. Serum-amylase was increased in 5 cases in addition to the 3 which presented as acute pancreatitis. The range was from 260 to 410 units.

Examination of the fæces in Groups 1 and 2 revealed ova of *Clonorchis sinensis* in 21 cases, those of *Ascaris lumbricoides* in 14, and of *Ankylostoma duodenale* in 11. In Group 3, while only 5 cases showed living adult flukes on dissection of the liver at autopsy, microscopical examination of the liver revealed evidence of previous infestation in a further 7 cases.

Table VI.—Analysis of the More Important Laboratory Findings

Jaundiced Cases		Pyrexial Cases				Alkaline Phosphatase (King-Armstrong Units)					
		Leucocyte Counts				Pyrexial		Pyrexia		Apyrexial	
Van den Berg (mg. per cent)		Range		Average		Not jaundiced		Jaundiced		Jaundiced	
Range	Average	Total (thousands/ c.mm.)	Polymorphs (per cent)	Total (thousands/ c.mm.)	Polymorphs (per cent)	Range	Average	Range	Average	Range	Average
2·1–8·5	3·4	10·5–29·2	76–96	16·2	87	7–42	30	23–97	42	7–38	27

Examination of the gall-bladders in these cases showed, at most, minimal macroscopical evidence of previous infection; those smaller than normal showed evidence of chronic inflammation. One case each in Groups 1-A and 1-B and 4 cases in Group 1-C had pyogenic empyema of the gall-bladder in the absence of obstruction to the cystic duct, the gall-bladders in these cases being virtually filled with pus.

Inflammatory involvement of the extrahepatic biliary tree as evidenced by gross thickening and pericholangeitis of the extrahepatic ducts was present in 56 of the 66 cases (85 per cent). In 38 cases (56 per cent) the extrahepatic ducts were dilated. In some cases the diameter of the common duct approximated to that of the duodenum. In only 10 cases was the appearance of the extrahepatic ducts normal. It should be noted that pericholangeitis was found in 15 of the cases with gall-stones confined to the gall-bladder, and in 5 of these there was coincidental dilatation of the extrahepatic ducts. Further, in Group 1-D in which no calculi were demonstrated, 9 cases showed pericholangeitis of varying severity, and in 4 of these the extrahepatic ducts were dilated. It should be emphasized that no matter how dilated the common duct was, and irrespective of the size of any contained gall-stones, the lower end of the duct was never stenosed and large sounds could be passed easily into the duodenum (*Fig.* 216 A, B).

Table VII.—Analysis of the Findings at Laparotomy

Group	No. of Cases	Size of Gall-bladder			Extrahepatic Bile-ducts			Macroscopic Biliary Cirrhosis	Pancreatic Fibrosis
		Enlarged	Normal	Small	Peri-choledochitis	Dilated	Normal		
Group 1	66	32	21	13	56	38	10	17	8
1-A	20	10	4	6	15	5	5	5	3
1-B	7	4	3	—	7	7	—	1	—
1-C	25	13	7	5	25	22	—	9	4
1-D	14	5	7	2	9	4	5	2	1

FINDINGS AT LAPAROTOMY

The salient findings at laparotomy are set out in *Table VII*. In 32 of the 66 cases (49 per cent) the gall-bladder was enlarged; in 20 (30 per cent) it was normal in size; and in the remaining 14 cases (21 per cent) it was smaller than normal. It should be noted that the gall-bladder was enlarged in 14 cases (52 per cent) in Groups 1-A and 1-B in which stones were found in that organ, and in 7 cases (26 per cent) it was normal in size. In 2 cases only, 1 case in each group, were stones impacted in the cystic duct. Those gall-bladders which were enlarged or normal in size showed, at

The surface of the liver at laparotomy in 17 cases presented the appearance of established biliary cirrhosis, and this diagnosis was confirmed by biopsy. It should be noted that 5 of these cases belonged to Groups 1-A and 2 to Group 1-D. In 3 cases there were large hyperplastic nodules.

Gross lymphadenitis especially affecting the glands towards the free margin of the gastrohepatic omentum was commonly encountered.

In 8 cases the pancreas on palpation was found to be unduly hard.

BACTERIOLOGY

Specimens of bile obtained at laparotomy from the gall-bladder or common duct in 63 of the 66 cases in Group 1 were cultures aerobically and anaerobically. *Table VIII.* A positive culture was obtained in 50 cases in Group 1 (79·4 per cent). *B. coli* alone was isolated in 41 cases, *B. coli* and an anaerobic streptococcus in 3, and anaerobic streptococcus and *S. typhi* in 1 case each, and *S. paratyphi B.* and *B. pyocyæus* in 2 cases each. In Group 2 a positive culture was obtained in 4 of the 11 cases (36·4 per cent). In 3 cases the organism was *B. coli* and in the remaining case an anaerobic streptococcus.

A B

FIG. 216.—A, A relative stricture of the common duct has formed above a large calculus. Note the gross dilatation of common hepatic and intrahepatic ducts. The stricture required dilatation to allow of removal of the stone. B, Stone removed, absence of stenosis of lower end of common duct evident. Upon relief of obstruction in the extrahepatic ducts the latter tend more readily to regain their normal calibre than do the intrahepatic ducts.

In Group 1-A the bile was obtained from the gall-bladder, whereas in Groups 1-B, 1-C, and 1-D it was obtained from the common duct. In 11 of the 24 cases in Group 2 the specimen of liver obtained by aspiration needle biopsy was divided and one portion, together with the fluid in the syringe, was inoculated into broth, the fragment of liver being first broken up under aseptic conditions. The results in both groups together with the analysis of the results in the subdivision of Group 1 are set out in

PATHOLOGY

It became evident from study of the autopsy material that although there was indication of previous infection of the whole biliary tree the process had been by no means uniform. In the majority of cases changes were much more advanced over the distribution of one or more branches of

Table VIII.—BACTERIOLOGICAL FINDINGS

GROUP	NO. OF CASES	NO. EXAMINED	POSITIVE CULTURE	STERILE	B. COLI	ANAEROBIC STREPTOCOCCUS	B. PYOCYANEUS	S. TYPHI	S. PARATYHPI
Group 1	66	63	50	13	44*	4*	2	1	2
1-A	20	18	11	7	8	1	—	1	2
1-B	7	7	6	1	6	1	—	—	—
1-C	25	25	23	2	23	1	—	—	—
1-D	14	13	10	3	7	1	2	—	—
Group 2	24	11	4	7	3	1	—	—	—

* In 3 cases *B. coli* and an anaerobic streptococcus were coincidentally isolated.

one of the hepatic ducts. Further, although the terminal acute suppurative cholangeitis involved the whole biliary tree, it was manifestly of longer standing in part of one lobe. This selective involvement was even better seen in the biopsies of the liver in Group 1. Frequently there was an absence of correlation between the aspiration needle biopsy and that obtained a few days later at laparotomy in the same case when the specimen could be taken from a selected area. In some cases when the needle biopsy revealed microscopically normal liver tissue the laparotomy biopsy showed severe and extensive changes. The histological appearances also varied within the segment of distribution of the infected duct. Sections from adjacent areas might show in one the appearances of bile retention, with little evidence of infection, and in the other that of a purulent cholangeitis.

The study of the pathological process in the larger branches of the biliary tree has been restricted to the autopsy specimens supplemented by cholangiograms, whereas that in the smaller ducts has been made on both the autopsy and biopsy material. It must be emphasized that the changes to be described were the same whether calculi were or were not present.

In the earliest phase of involvement of the smaller radicles of the biliary tree the lumen of the duct is filled with pus (*Fig.* 217). Rapid extension occurs into the surrounding tissue, with destruction of the duct (*Fig.* 218). A prominent feature in the early lesion is a marked dissociation of the liver cells due to infiltration of the sinusoids with polymorphonuclear leucocytes together with hyperplasia of the Kupffer cells. A varying degree of cellular necrosis, either peripheral or centrilobular in distribution, is encountered in the lobules around the affected duct. Resolution, spontaneous or following treatment with antibiotics, results in replacement of the miliary abscesses by dense round-cell infiltration, in turn succeeded by formed fibrous tissue in which numerous bile-ducts appear (*Fig.* 219). Repeated cycles of infection and resolution result in a monolobular cirrhosis.

In the larger intrahepatic ducts there is marked inflammation of the duct wall and the lumen is filled with pus and desquamated epithelium (*Fig.* 220). The infection extends to the surrounding

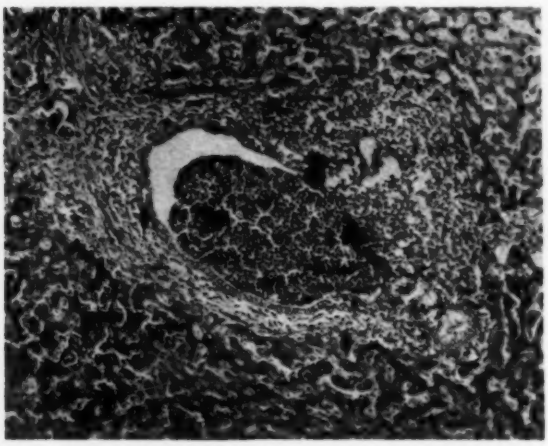


FIG. 217.—Early stage of an exacerbation of recurrent pyogenic cholangeitis as it affects the smaller branches of the biliary tree.

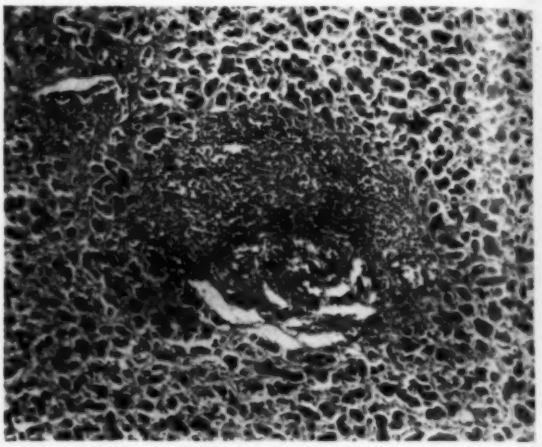


FIG. 218.—Later stage than *Fig.* 217 of an acute exacerbation.

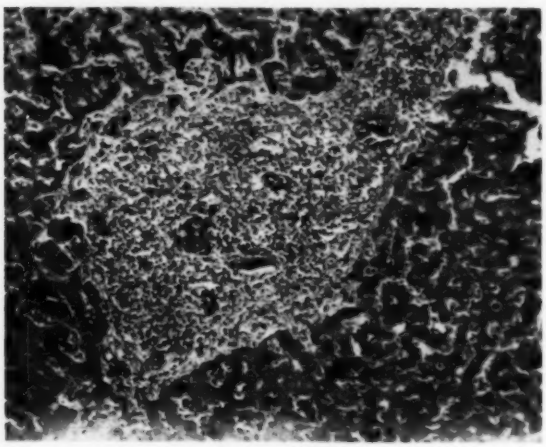


FIG. 219.—Stage of remission.

FIG. 220.—Acute exacerbation as it affects larger branches of the biliary tree.

tissue, with the irregular formation of miliary abscesses around the duct. Resolution results in fibrosis and is responsible for the undue prominence of the duct wall seen on section of the liver. Repeated cycles of infection and resolution produce trabeculæ of fibrous tissue, more prominent towards the confluence of larger ducts, which extend irregularly into the liver parenchyma. In these trabeculæ branches, both of the portal vein and of the hepatic artery respectively, show endophlebitis and endarteritis in varying degree.

During the acute infection the lumen of the larger intrahepatic ducts may become irregular in calibre. Short segments of relative stenosis due to inflammatory reaction in the wall may occur at intervals along a duct (*Figs.* 221, 222). The duct proximal to the stenosis dilates. As a result of recurrent infection there is permanent damage to the walls of the ducts, for in the majority of cases, including those in which no calculi were found, the ducts remain dilated. This dilatation is well seen in the accompanying cholangiogram (*Figs.* 222, 223). In many cases localized strictures can be demonstrated, and these were most frequently encountered at the confluence of two ducts (*Fig.* 224).

FIG. 221.—Short segments of relative stenosis apparently confined to an inferior branch of the right posterior hepatic duct. Small negative shadow seen in middle portion possibly due to early calculus formation.

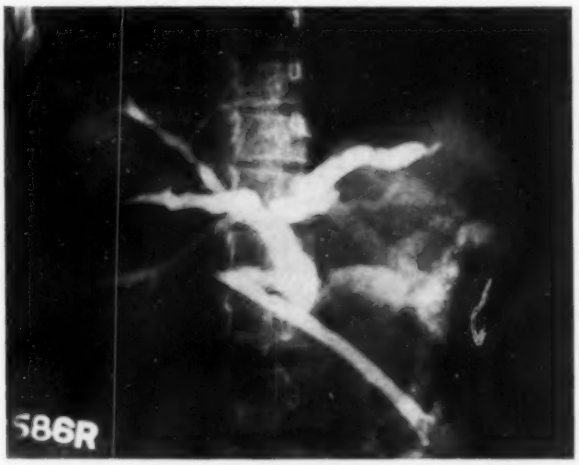


FIG. 222.—Short segments of relative stenosis evident in several dilated intrahepatic ducts. One large calculus had been removed from the gall-bladder. No other calculi demonstrable in the biliary tree.

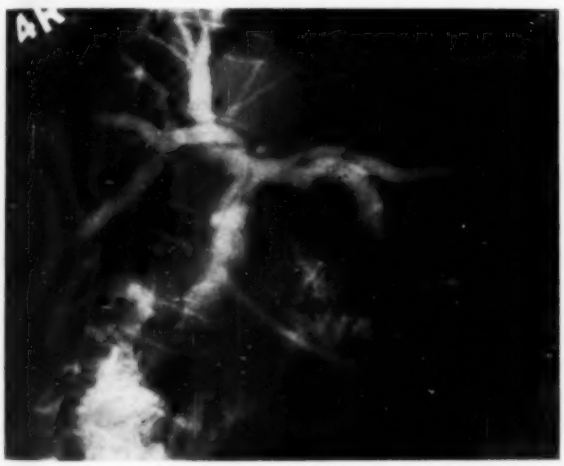


FIG. 223.—At operation the gall-bladder was apparently normal and the common duct contained two stones, which were removed. The post-operative cholangiogram shows a greatly dilated biliary tree apparently free from stones.

FIG. 224.—Note the relative stricture (indicated by white arrow) at the confluence of two major ducts which are dilated. The large negative shadow in the greatly dilated branch of the left hepatic duct is presumably due to biliary mud or calculi. Stones had been removed from the common duct at operation.

Should resolution not occur confluence and direct extension result in the formation of macroscopical abscesses of varying size. Solitary large abscesses may result from intrahepatic suppurative thrombophlebitis of a branch of the portal vein, with rapid extension over the area of distribution involved.

ANALYSIS OF STONES

The calculi removed at operation and a selection of those obtained at autopsy were subjected to analysis. The results of this analysis are set out in *Table IX*. For convenience stones with a cholesterol content of more than 10 per cent will be described as 'mixed' stones, and those with a cholesterol content of less than 10 per cent as 'bilirubin' stones. From *Table IX* it will be seen that the stones in 4 cases in Group 1-A and 1 case in Group 1-B may by this standard be described as mixed. The stones in the remaining cases were bilirubin stones.

The mixed stones in the gall-bladder in Groups 1-A and 1-B were of a reasonable dimension, the largest, a solitary stone, weighed 5·5 g. In 2 of the 5 cases the stones were solitary, and in the remaining cases there were 7, 8, and 12 stones respectively. These multiple stones were faceted with the exception of the case in Group 1-B, in which they were spherical and had a nodular surface.

The bilirubin stones in the gall-bladder in both groups varied widely in size. The largest, a solitary stone, weighed 3·58 g. In 4 of the 20 cases of Groups 1-A and 1-B the stones were solitary, in 1 there were two stones and in 14 more than two; the largest number in one case was twenty-seven. In the remaining case the gall-bladder was filled with inspissated bile having the consistency of thick mud, which was shown to consist almost entirely of bile-pigment, with only traces of calcium and cholesterol. In shape the bilirubin stones varied from small irregular scale-like plaques to spherical structures. In most the surface was smooth, but occasionally rounded stones had a mulberry-like surface. In the main the small stones were hard, and on drying had a polished appearance, but some of the smaller and the majority of the larger calculi had a hard outer layer with a soft centre, and these could be crushed readily between the finger and thumb. After drying, the hard surface had the appearance of earthenware and tended to flake off—the 'earthy' stones of Aschoff (1924).

The mixed stones encountered in the common duct in one case in Group 1-B were rounded with a nodular surface similar to those found in the gall-bladder in the same case.

In the remaining cases of calculi in the extrahepatic biliary tree the stones were bilirubin stones which varied widely in size and numbers. The largest stone, a solitary one, weighed 10·2 g., was egg-shaped, and measured 5 cm. in length and 2·6 cm. at its greatest diameter. In 5 cases the stones were solitary, in 2 there were two stones, and in the remainder with two exceptions there were more than two. In 3 cases a widely dilated common duct contained large numbers of small irregular stones. The two exceptions had no formed calculi, but the dilated common duct contained a large quantity of thick biliary mud. Biliary mud was occasionally encountered in association with formed calculi. Although many of the smaller calculi were hard, the majority could readily be crushed between finger and thumb. The larger calculi invariably had the hard outer surface and the crumbling centre of inspissated biliary mud described above. When dried, the scaling of the surface was even more marked and the appearance was rather akin to dark, decayed wood.

The stones found in the intrahepatic ducts at autopsy were essentially similar to those found in the extrahepatic ducts. In size they varied widely from minute rounded calculi to stones 2 cm. or more in diameter. They were not infrequently egg-shaped

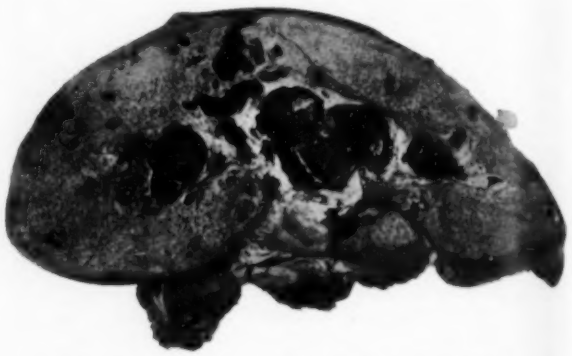


FIG. 225.—Transverse section of the liver showing intrahepatic calculi. Note the isolated single calculi in the periphery. (× ½ approx.)

Table IX.—CHEMICAL ANALYSIS OF CALCULI

GROUP	NO. OF CASES	RANGE PER CENT			AVERAGE PER CENT			NO. RADIO-OPAQUE
		Cholesterol	Bilirubin	Calcium	Cholesterol	Bilirubin	Calcium	
Group 1-A, 20 cases	4	35·0–80·0	17·5–64·5	0·5–10·0	62·3	32·5	3·75	2
	15	0·5–10·0	73·0–98·5	0·5–30·0	2·3	88·0	8·7	10
Group 1-B :—								
a. Gall-bladder stones	1	85·0	14·5	0·5	—	—	—	—
	6	1·0–10·0	88·0–96·5	0·5–21·0	3·25	88·9	7·0	3
b. Extrahepatic duct stones	1	80·0	19·0	1·0	—	—	—	—
	6	0·5–10·0	88·0–98·5	0·5–4·0	3·1	94·0	2·1	2
Group 1-C, 25 cases	19	0·5–7·0	91·0–99·0	Trace to 3·8	2·1	95·1	1·7	5
Group 3, 20 cases	4	0·5–2·0	93·0–98·0	Trace to 1·4	1·1	96·2	0·7	—

with the long axis lying in the axis of the dilated bile-duct. In a single liver slice the number of stones might vary from one to two to large numbers (*Fig.* 225). In many cases one or more localized dilatations of the biliary tree contained inspissated biliary mud. This occurred alone in 2 cases, but was more usually encountered in association with formed calculi elsewhere in the intrahepatic biliary tree. The formed stones had the thin hard external layer which flaked on drying and a soft core of nuclear calculus found. Little pigment could be extracted from fragments of the scaling layer by chloroform unless it was first treated by diluted acid, whereas pigment could readily be extracted from the laminæ without such treatment.

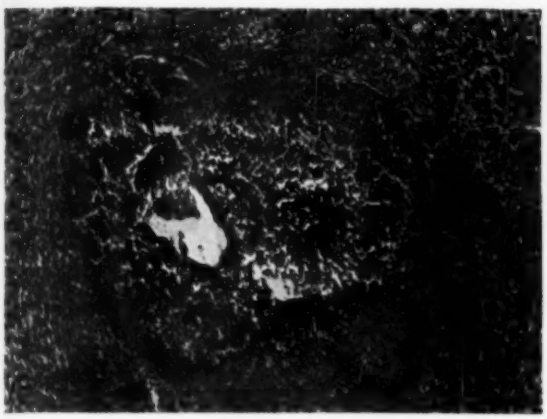


FIG. 226.—Impregnation of pus by bile-pigment to form intrahepatic biliary mud.

FIG. 227.—Formed intrahepatic bilirubin stone. Note the laminated structure around the central nucleus of inspissated biliary mud.

FORMATION OF CALCULI

The contention of Digby (1930) that stones found in the common duct formed initially in the intrahepatic ducts appears to be untenable. Stones may occur in the common duct in the absence of intrahepatic calculi. Further, intrahepatic formation would not account for the presence in the gall-bladder of stones almost identical in structure to those occurring in the common duct. It so chanced that none of Digby's 15 cases had stones in the gall-bladder. Finally, in the majority of cases, intrahepatic stones are held in localized dilatations of the bile-ducts, and since the diameter of the stone is greater than the diameter of the duct distal to it, the stone cannot readily pass down into the larger ducts. We must, however, admit the possibility of ulceration of the stone into the larger duct. It would appear, in view of the high proportion of positive bile cultures, that the stones in the gall-bladder and common duct, like the intrahepatic stones, are septic formations.

A study of the autopsy material reveals various stages in the development of intrahepatic calculi, and from these a composite picture of the formation of such calculi can readily be built up. Pus, and in the larger ducts epithelial debris, retained within the lumen of the duct as a result of partial obstruction consequent upon cholangeitis becomes impregnated with bile-pigment (*Fig.* 226). Further impregnation results in the formation of biliary mud from which calculi arise (*Fig.* 227). The calculi which form in the smaller bile-ducts are limited to a few millimetres in size. They may be found in any part of the liver, but are best seen towards the periphery, where they are the only calculi encountered, and although multiple each is isolated from the other. Since these calculi consist of bile-pigment, and since they are larger than the diameter of any duct in the periphery of the liver, it would

inspissated biliary mud. Occasionally small calculi were hard, but the majority of stones could readily be crushed. In many cases the stones were restricted to one lobe or part of a lobe, while in others they occurred irregularly throughout the liver.

When the small hard calculi from both the gall-bladder and bile-ducts were crushed, only traces of pigment could be extracted by chloroform, but following treatment with acid the pigment was readily soluble in chloroform. In contrast the greater part of the pigment could be extracted from the small soft stones by chloroform alone. Treatment of the washed residue with acid and further extraction with chloroform yielded a variable but small amount of pigment. It would appear, therefore, that the small hard calculi consisted largely of calcium bilirubinate, whereas the soft calculi consisted mainly of bilirubin in the free state.

Some 20 of the smaller soft calculi from the biliary tree were subjected to the prolonged action of acid alcohol. After such treatment a cloud-like structure of organic material was obtained. In 19 of the specimens microscopical examination gave no clue as to the origin of this organic material. The residue of the remaining specimen, a soft calculus, after treatment with acid alcohol was recognizable as a partially disintegrated adult *Clonorchis sinensis*.

Section of the dried larger bilirubin stones was difficult because of their friable nature. The central mass in each stone examined was large, uniform in appearance, and friable. Surrounding this mass were laminæ of varying thickness but of uniform earthen appearance similar to the central mass. Each lamina was separated by a thin layer identical with the superficial scaling layer. In no case was a

appear that during their formation complete obstruction to the duct is not produced. The limitation in size is probably imposed by destruction of the liver parenchyma drained by the duct in which the stone forms.

The calculi in the larger intrahepatic ducts may reach 2 cm. or more in diameter. As they increase in size they do not produce complete obstruction,

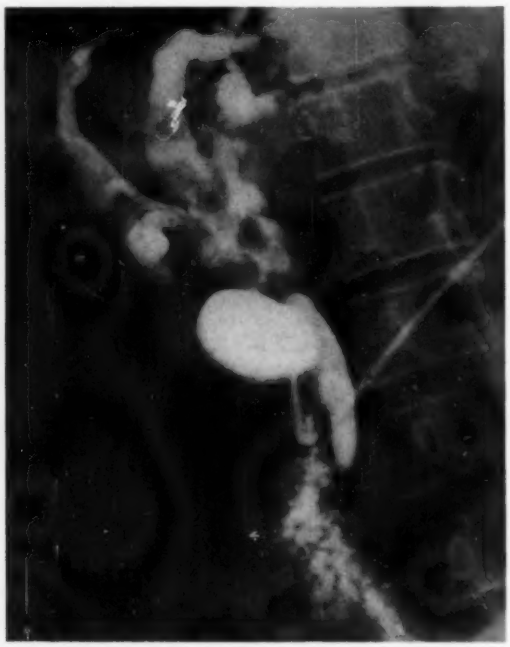


FIG. 228.—Cholangiogram through cholecystostomy tube showing stones confined to the common hepatic and intrahepatic ducts. Many of the stones seen were subsequently removed.

for although the duct proximal to the stone dilates it still contains bile. In the dilated duct behind the primary stone biliary mud and smaller calculi appear, and as the stones increase in size and numbers the duct becomes greatly dilated. Invariably the primary calculus retains its position in advance of the others.

The lumen of a major intrahepatic duct may be partly occluded by a calculus forming in a small duct close to it. The major duct proximal to the compression dilates and secondary stones may form therein.

Occasional cases have been encountered in which calculi fill the extrahepatic ducts and extend into the main intrahepatic ducts. This process is of importance since intrahepatic stones so formed, in contrast to most primary intrahepatic stones, can be removed at operation (*Fig.* 228).

While there is no doubt that suppurative cholangeitis is the usual precursor of intrahepatic stone formation, there is reason to believe that, in those cases with evidence of infestation by *Clonorchis sinensis*, some of the stones might be of aseptic formation. McFadzean and Huang (1954) during observations on experimental infestation of guinea-pigs with *Clonorchis sinensis* found collections of biliary mud and minute calculi in the intrahepatic bile-ducts which were the seat of varying degrees of stenosis produced by reaction to the parasite. In none of the animals was there evidence of infection. Since this fluke also produces partial obstruction in the intrahepatic bile-ducts in man it may well be that some of the calculi in our cases so infested arose as aseptic formations. Even in this event secondary infection must follow, for we have not yet encountered intrahepatic stones in the absence of suppurative cholangeitis.

So far we have considered the method of formation of intrahepatic stones. Similar processes result in the formation of bilirubin stones in the extrahepatic ducts and in the gall-bladder. In the presence of pyogenic infection and concomitant bile stasis biliary mud is formed. Stasis and infection in the case of the gall-bladder are provided by obstruction at the lower end of the common duct which results in the damming back of infected bile. In our series cases have been encountered in which the common duct or gall-bladder was filled with thick mud. From this mud bilirubin stones are formed. Once the initial common-duct stone has formed, repeated exacerbation of the infection results in the deposition of further layers of biliary mud which, on becoming inspissated, lead to the laminated appearance of the stone. It would appear reasonable to assume that the thin hard layers of calcium bilirubinate correspond to periods of quiescence. In its growth the stone is moulded by the common duct which enlarges *pari passu* (*Fig.* 229). Proximal to the primary stone, secondary stones may form.

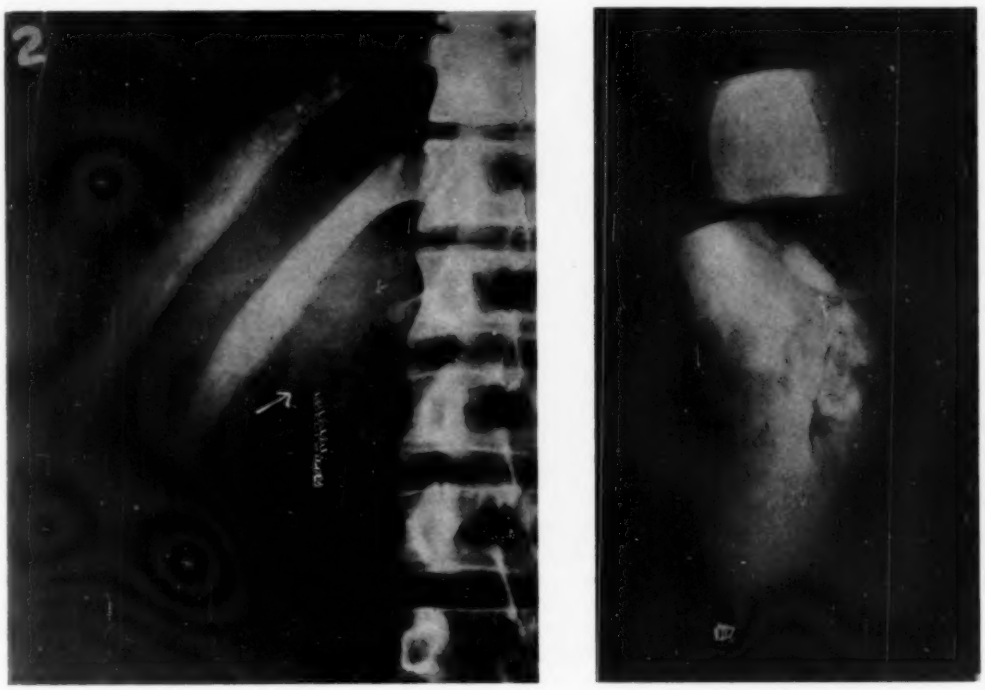
DISCUSSION

The majority of cases in Groups 1 and 2 gave a history of recurrent attacks of fever, and those cases investigated during such an attack showed findings consistent with a pyogenic infection of the biliary tree. The uniformity of the clinical picture independent of the presence or absence of stones and independent of the distribution of stones indicates that a recurrent pyogenic cholangeitis was common to all. That this is indeed so is established by the findings on microscopical examination of liver biopsies in these cases and by the high proportion of positive bile cultures obtained in all subdivisions of Group 1. The high proportion of positive cultures (80 per cent) becomes the more impressive when one considers that antibiotics or sulphonamides had been given to all save one case prior to operation, which was performed in most cases in the stage of remission. It may be asserted, therefore, that among the Chinese in Hong Kong infection of the biliary tree plays a dominant role in gall-stone formation whatever the site. This assertion would appear to hold good in Japan in the cases with cholelithiasis reported by Miyake and Ishiyama (1930), who obtained a positive culture in a similar proportion of cases. In their series the most frequently isolated organism was again *B. coli*.

Since recurrent infection of the biliary tree was encountered in the absence of calculi, it seems reasonable to assume that such anticipates the development of calculi but, as is seen from the autopsy material, the condition may proceed to a fatal outcome without the development of stones. In the main, the shorter the history and the younger

the patient the less likely is the development of calculi. This is well seen in Groups 1-D and 3-C. The early age and short duration of history were the determining factors in denying laparotomy to 21 of the cases of Group 2.

If the 2 cases, 1 with a dilated and 1 with a normal-sized gall-bladder, with stones obstructing the cystic duct be excluded, 31 of the cases at laparotomy showed enlargement of the gall-bladder, and in 20 it was normal in size. In these 51 cases macroscopical evidence of previous cholecystitis was minimal. In 13 cases only was the gall-bladder chronically inflamed and smaller than normal. In contrast pericholangeitis was present in 56 cases, and in 38 of these the extrahepatic ducts were dilated. In Group 1-A in which stones were confined to the gall-bladder, again excluding the 2 cases of stones impacted in the cystic duct, the gall-bladder was enlarged in 9 cases and in 3 of the remainder it was of normal size. In 6 cases only was it fibrosed and contracted. In this group 15 cases gave evidence of pericholangeitis, and 5 of these had dilated ducts. These findings show that the brunt of the infection is borne by the bile-ducts and not by the gall-bladder. In European stock involvement of the gall-bladder is considered to be primary and that of the ducts secondary. Walters and Snell (1940) stated that 80 per cent of cases of choledocholithiasis have a fibrotic and functionless gall-bladder. This was encountered in only 5 (16 per cent) of the present series of 32 cases of choledocholithiasis. If the autopsy material be included the incidence was 15 per cent. Judd and Marshall (1931) analysed 738 consecutive cases of choledocholithiasis and found coincidental calculi in the gall-bladder in 65 per cent. In the present series only 22 per cent had coincidental stones in the gall-bladder. If the autopsy material is included the incidence was 21 per cent. The low incidence in all groups of fibrosed contracted gall-bladders and the high incidence of choledocholithiasis in the absence of a sclerosed functionless gall-bladder or gall-bladder stones suggest that in the Chinese in Hong Kong in contrast to Europeans the primary infection originates in the bile-ducts and that involvement of the gall-bladder is secondary. It is our view that with exacerbation of the choledochitis and resulting obstruction of the lower end of the common-duct infection extends to involve the gall-bladder, and it must be emphasized that this infection is primarily of the mucosa. While this usually resolves with little damage to that organ, in a minority of cases the inflammatory process extends to involve the entire gall-bladder wall, leading ultimately to fibrosis and contraction of that organ. Bilirubin stones may or may not be formed in either case. It should be noted that extension of infection to the gall-bladder may also result in the production of a true empyema in the absence of calculus obstruction to the cystic duct. This was encountered in 6 cases (1 each in Groups 1-A and 1-B, and 4 in Group 1-C). The hypothesis that the gall-bladder is involved as a result of extension of infection from the common duct would explain the minimal degree of cholecystitis in the majority of cases and the frequent apparent breach of Courvoisier's law. Further, it would explain the high incidence of jaundice in cases of Group 1-A.



A B

FIG. 229.—A, Straight radiograph showing large common duct stones. B, Radiograph of stones after removal. (Natural size.)

The nature of the stones found in the gall-bladder affords additional evidence in favour of our belief that the gall-bladder infection is secondary to that of the bile-ducts. Many of the bilirubin stones were identical with the 'earthy' stones described by Aschoff (1924) as arising in the common bile-duct as the result of stasis. Aschoff considered that similar stones might rarely arise in the gall-bladder "when this has lost its protective valve, the narrow wound cystic duct". Such an occurrence can readily be envisaged in the course of extension of infection from the bile-ducts to the gall-bladder, but in this community it must be regarded as a commonplace and not the rarity it was considered to be by Aschoff.

In those cases showing dilatation of the extrahepatic bile-ducts in the absence of calculi or organic stricture it is conceivable that calculi previously present in the common bile-duct had passed into the duodenum. This seems unlikely to apply to all such cases. A second possibility is that a functional obstruction is responsible. Distension of the bile-ducts occurs in hypertonic biliary dyskinesia and, among others, Elkeles and Mirizzi (1942) have reported its occurrence as the result of inflammatory involvement of the sphincter of Oddi. The evidence at our disposal suggests that the obstruction is of inflammatory origin.

Since the evidence indicates that the calculi in our cases are of infective origin, the results of the chemical analysis of the stones are of great interest. While we have chosen to describe all stones with cholesterol content greater than 10 per cent as mixed stones, it should be noted that Pickens, Spanner, and Bauman (1932) gave the average composition of mixed stones as cholesterol 94 per cent, bile-pigment 3·26 per cent, and calcium 1·09 per cent. The average pigment content of the stones in 6 cases described as mixed was 27·5 per cent, the lowest being 14·5 per cent and the highest being 65·4 per cent. Structurally these stones were not 'combined' stones, consequently the mixed stones in our series have an unusually high content of pigment and might more properly be described as bilirubin stones with high cholesterol content. The majority of stones were pigment stones with a low cholesterol content, and they may be divided into three groups: a small hard stone consisting largely of calcium bilirubinate; a soft stone consisting of bilirubin; and one which contained both. The last was the commonest, but all three forms of calculi were frequently encountered together in the same case. In the main it may be stated that calcium-bilirubin stones occurred more frequently in the gall-bladder than in the common duct, in which they were more common than in the intrahepatic ducts.

Bilirubin stones, the 'earthy' stone of Aschoff (1924), have frequently been recorded as arising in the common duct as the result of stasis, but under such circumstances there is usually a nuclear calculus. Such a calculus was not encountered in the present series. Calcium-bilirubinate stones have been regarded as aseptic formations of metabolic origin occurring usually in the course of congenital spherocytic hæmolytic anæmia. They have, however, been encountered in other forms of hæmolytic anæmia—for example, they have been reported in sickle-cell anæmia in negroes. There was no evidence of hæmolysis in our series and only 7 of the 90 cases had a history of malaria. It must be assumed, therefore, that the calcium bilirubinate stones were also of infective origin. The greater content of calcium bilirubinate in stones in the gall-bladder suggest that available calcium may well determine their occurrence. It should be noted that 79·75 per cent of the cases of cholelithiasis reported from Japan by Miyake and Ishiyama (1930) had bilirubin stones, and there was in this series a high incidence of infection.

The restriction of infection within the liver to a part of the biliary tree, as seen in the clinical material, suggests a blood-borne rather than an infection ascending from the duodenum. This suggestion is supported by the report of McFadzean, Chang, and Wong (1953) of an unusually high incidence in Hong Kong of solitary pyogenic abscess of the liver due to *B. coli*. These abscesses were most frequently encountered in the first three decades, an incidence similar to that of the onset of symptoms in our cases. The solitary abscesses were classified as cryptogenic, but the clinical and laboratory evidence was considered to indicate that they resulted from portal bacteriæmia.

If it is assumed that the organisms producing recurrent pyogenic cholangeitis reach the liver via the portal vein, then some factor must determine their localization to the biliary tree. This has not been determined. Any condition producing bile stasis would achieve this. In Hong Kong and in Japan there is a high incidence of infestation of the bile-ducts with *Clonorchis sinensis*, and adult flukes can produce partial or complete obstruction of radicles of the biliary tree. Although examination of the fæces failed to show ova in the majority of cases (77 per cent), this may not be of significance since infection of the biliary tree results in death of the flukes. Previous infestation, however, invariably leaves microscopical changes in the walls of the intrahepatic ducts. Study of the 20 cases in Group 3 showed no evidence of previous infestation in 45 per cent. It would seem, therefore, that while infestation by *Clonorchis* may well play a part in some cases, it cannot account for all of them. It would appear reasonable to assume that once infection has occurred the pathological changes will predispose to further infection, especially if calculi have formed. It should be noted that no cases of calculi either in the intrahepatic or extrahepatic ducts have been encountered without evidence of pyogenic cholangeitis.

Evidence suggesting that an ascending infection of the ducts from the duodenum might have occurred was encountered in only 2 cases, both in Group 1-C. In 1 case a live adult *Ascaris lumbricoides* was found in the common bile-duct. That an ascending infection of the biliary tree results from its invasion by ascaris is recognized the world over (Rolleston and McNee, 1929), and has been the subject of a number of communications from China. Miyake and Ishiyama (1930) reported that in 12·75 per cent of all their cases of cholelithiasis, bilirubin calculi formed on a nucleus of an adult ascaris which had invaded the biliary tree. Since only 15 per cent of our cases had ova isolated from the fæces, it is highly

improbable that invasion of the ducts by ascaris played a part save in the exceptional case. Further, the calculi described by Miyake and Ishiyama (1930) are readily recognized and none were encountered in the present series. In the second case a straight

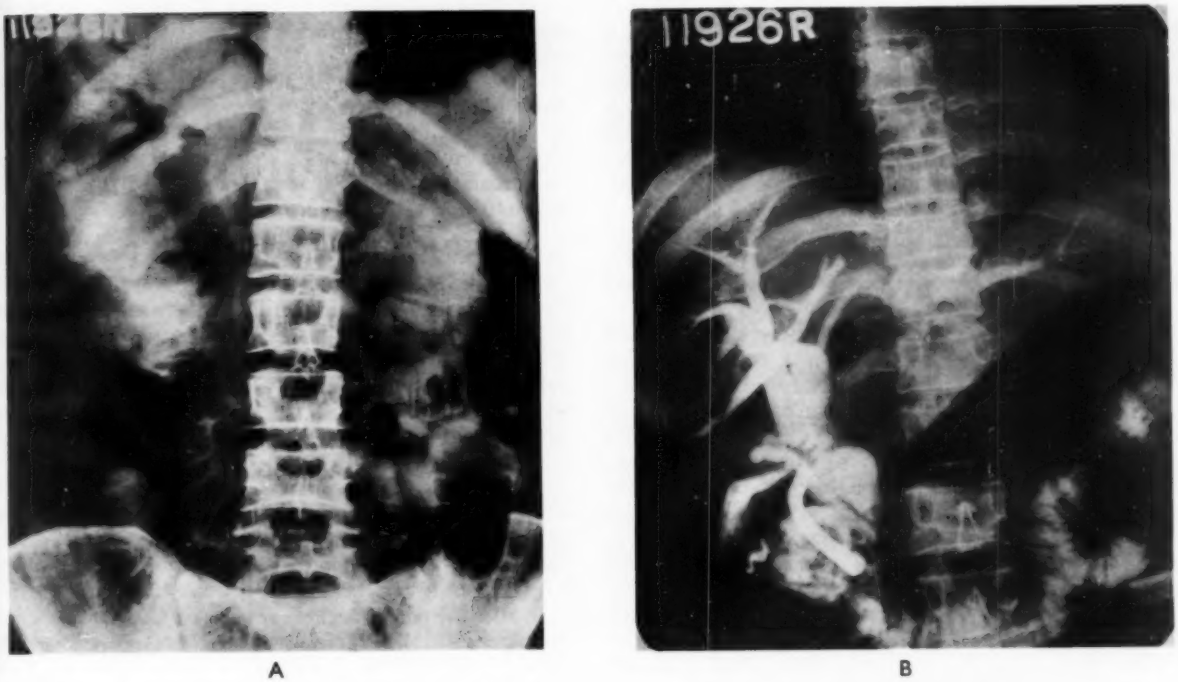


FIG. 230.—A, Pre-operative radiograph showing a dilated biliary tree filled with gas. B, Post-operative cholangiogram duplicates A. Two soft stones and much biliary mud had been removed from the common duct. C, Barium meal demonstrating filling of lower portion of common duct from the duodenum.

radiograph of the abdomen had shown gas in the biliary tree and a barium meal ascending filling of the common duct. There was no internal biliary fistula in this case (*Fig.* 230).

TREATMENT

In those cases admitted during an acute exacerbation of the disease, treatment was initially directed towards acceleration of the remission, which would occur sooner or later spontaneously in the majority of instances. Rapid control of the acute infection was achieved by antibiotics, aureomycin, chloramphenicol, and streptomycin proving effective. Sulphadiazine was less effective. Measures calculated to facilitate drainage of the biliary tree were coincidentally employed in cases of all groups. Nitroglycerin was administered sublingually, atropine subcutaneously, and dehydrocholine by mouth. As soon as it could be tolerated a high-protein, high-carbohydrate diet was given. This is of major importance, since many of our patients were of poor nutritional status. Parenteral vitamin K was given as a routine.

Our view that the infection which gives rise to gall-stones has its origin in the liver and not in the gall-bladder is reflected in the operative treatment.

The primary object of surgical intervention is the removal of accessible stones and drainage of the biliary tree. In view of the significant number of cases subjected to operation in which no stones were demonstrated, we held the opinion that laparotomy was unjustifiable in those cases in younger age groups in which the history was of short duration. Upon reviewing our findings we now consider that this attitude was unduly conservative, and the wiser course would be to perform a laparotomy and cholangiography to exclude beyond doubt the presence of stones in the accessible ducts. Cholangiography is manifestly essential following removal of

stones in order to determine whether their removal has been complete. Further, the technique employed, which will be described in a separate paper, should be such as to fill the intrahepatic as well as the extrahepatic ducts.

In European stock the case for cholecystectomy is established, since the gall-bladder is primarily involved, is commonly cicatrically contracted, and is the focus which maintains infection in the biliary tree. In our cases, however, the gall-bladder is more sinned against than sinning, and we hold the view that the only indication for cholecystectomy is irremedial damage to the gall-bladder. We agree with Digby (1930) that the conservation of the gall-bladder is of importance, since its presence affords a safety-valve usefulness which will delay the onset of suppression of bile in the event of recurrence of obstruction which is to be anticipated in the majority of cases.

All attempts to eradicate infection have failed. The administration of antibiotics and sulphonamides prior to operation, although controlling the acute exacerbation, do not sterilize the biliary tree, as witness the high proportion of cultures at laparotomy following such treatment. It would appear reasonable to assume that the effect exerted on the acute exacerbation results from control of the extension of the infection from the ducts into the parenchyma, and of the acute choledochitis superimposed on the chronic-duct infection in cases with extrahepatic stones. Prolonged drainage of the biliary tree through a T-tube had no apparent effect other than to decompress the biliary tree, since bile cultures remained positive following removal of stones from the extrahepatic ducts in spite of coincidental courses of antibiotics. In view of the ease with which contrast medium could be introduced even into the finer branches of the biliary tree, local instillation of antibiotics coupled with systemic administration were tried. Bile cultures remained positive for as long as twenty-eight days. It is manifest, therefore, that the pathological changes in the liver, with or without the formation of intrahepatic calculi, are responsible for the maintenance of an infection which does not yield to existing treatment. Obviously the ideal in treatment is prevention of the pathological changes which serve to maintain infection, but this can only be achieved when the factors responsible for the initial vulnerability of the bile-ducts to infection are determined and corrected. If infestation with *Clonorchis sinensis* plays a part, prevention or early eradication of the infestation is essential. The former lies outwith our province. Available treatment of the infestation is ineffective, although the observations of McFadzean and Huang (1953) indicate that hexachloroethane may well prove effective in early infestation before gross secondary changes in the biliary tree have occurred.

PROGNOSIS

There have been no operative deaths in the series. One case died ten weeks after operation. In this case the extrahepatic ducts had been found greatly thickened and dilated but contained no stones. The gall-bladder appeared normal and cholangiography confirmed the absence of stones in the extrahepatic ducts, but demonstrated numerous intrahepatic stones. *B. coli* was isolated on culture of the bile from the common duct. The post-operative course was uneventful and she was discharged from hospital. The patient was re-admitted six and a half weeks after operation with an acute exacerbation which could not be controlled by antibiotics. At autopsy no stones were found in the extrahepatic ducts, but there were numerous intrahepatic stones with multiple abscess formation.

In the remaining cases the follow-up has not been sufficiently long to allow of assessment, but it is our opinion that, unless infection dies out, with existing antibiotics and chemotherapeutic agents, the prognosis is poor and recrudescence of the infection inevitable.

SUMMARY AND CONCLUSION

There is presented a study of 110 cases of a syndrome in which the findings were consistent with recurrent pyogenic infection of the biliary tree. This infection originated not as a sequel to cholecystitis, as is the case in Europeans, but as a primary pyogenic cholangeitis. For convenience the syndrome is referred to as recurrent pyogenic cholangeitis.

The syndrome consists essentially of recurrent and variable attacks of fever, of right upper abdominal pain either lancinating or colicky in character, and of jaundice. The liver and gall-bladder are commonly palpably enlarged, and there is a variable leucocytosis. The alkaline phosphatase is elevated and, in jaundiced cases, this rise is greater than that to be expected from the degree of jaundice.

The infection has an approximately equal sex incidence, and although no age group would appear to be exempt, the onset is, in the main, in the younger ages.

The dominant organism is *B. coli*, and the evidence indicates that the infection is initially conveyed by the portal vein to the liver, but the factor or factors responsible for its localization there are as yet undetermined. A descending infection of the biliary tree results. Once established the condition has periods of exacerbation and remission. During periods of exacerbation obstruction to the common duct from spasm or calculus occurs with consequent bile stasis. This may result in secondary infection of the gall-bladder and in aggravation of the disease process in the liver. While the condition must be regarded as a total involvement of the biliary tree, the brunt of the infection may be borne by the liver, by the major extrahepatic ducts, or by the gall-bladder.

The combination of bile stasis and infection results in conditions conducive to the formation of calculi in the extrahepatic ducts, in the intrahepatic ducts, and in the gall-bladder. It should be noted, however, that the disease may progress to a fatal issue without the formation of calculi. The stones, independent of the site of formation, are almost invariably bilirubin stones.

Since the infection has an almost equal sex incidence, the complicating cholelithiasis occurs equally in the sexes. This is in contrast to the findings in Europeans in whom there is a dominant incidence in females. Again, since primary pyogenic cholangeitis has its onset in the earlier age groups, the

complicating stones in the bile-ducts also occur in younger age groups. In Europeans stones in the bile-ducts are secondary to gall-bladder disease, which has its maximum incidence in the fifth decade, consequently the main incidence of choledocholithiasis is in decades later than the fifth. The incidence of gall-bladder stones occurs in the same age groups in Europeans and in Hong Kong Chinese, but this is to be expected since, in the Chinese, gall-bladder involvement is secondary to cholangeitis, that in Europeans being a primary condition.

The general picture presented is that of Charcot's intermittent hepatic fever, this irrespective of the complications which may occur in any given case. While this is so it will be appreciated that the Hong Kong Chinese are especially liable to primary pyogenic cholangeitis and that the resulting pathology is gross in the extreme. It is not possible on clinical grounds to exclude the presence of stones in the extrahepatic ducts, and for that reason we consider that laparotomy is indicated in all cases in the event of recurrence. Removal of the stones and decompression of the biliary tree is certainly not curative, but may well be expected to prolong life.

We have pleasure in acknowledging the assistance given us by Mr. K. T. Liu, who was responsible for the chemical analysis of the gall-stones; by Dr. C. T. Huang, who did some of the bacteriological investigations; and by Majors P. D. Stewart and H. C. Jeffrey, R.A.M.C., who performed many of the biochemical investigations. Finally, we have to thank Mr. C. T. Yung, Chief Technician, Department of Pathology, University of Hong Kong, for the photomicrographs and reproductions of radiographs submitted with the paper.

REFERENCES

ADAMS, R., and STRANAHAN, A. (1947), *Surg. Gynec. Obstet.*, **85**, 776.
ASCHOFF, L. (1924), *Lectures on Pathology*. New York: P. B. Hoeber Inc.
BOCKUS, H. L., WILLARD, J. H., and METZGER, N. H. (1935), *Penn. med. J.*, **39**, 482.
DESSAU, F. I. (1943), *New Engl. J. Med.*, **229**, 464.
DIGBY, K. H. (1930), *Brit. J. Surg.*, **17**, 578.
— — (1934), *Trans. 9th Congr. Far East Ass. trop. Med., Nanking*, **2**, 951.
ELKELES, G., and MIRIZZI, P. L. (1942), *Ann. Surg.*, **116**, 360.
GLENN, F. (1947), *Rev. Gastroent.*, **14**, 240.
JUDD, E. S., and MARSHALL, J. M. (1931), *Arch. Surg., Chicago*, **23**, 175.
LITTLER, T. R., and ELLIS, G. R. (1952), *Brit. med. J.*, **1**, 842.
MARSHALL, S. F., and PHILLIP, E. S. (1948), *Surg. Clin. N. Amer.*, **28**, 633.
MIYAKE, H., and ISHIYAMA, F. (1930), *Dtsch. Z. Chir.*, **225**, 187.
MCFADZEAN, A. J. S., CHANG, K. P. S., and WONG, C. C. (1953), *Brit. J. Surg.*, **41**, 141.
— — and HUANG, C. T. (1954). In preparation for the press.
PICKENS, M., SPANNER, G. O., and BAUMAN, L. (1932), *J. biol. Chem.*, **95**, 505.
ROBERTSON, H. E. (1945), *Gastroenterology*, **5**, 345.
ROLLESTON, H., and MCNEE, J. W. (1929), *Diseases of the Liver*, 3rd ed. London: Macmillan & Co.
RUFANOV, I. G. (1936), *Ann. Surg.*, **103**, 321.
WALTERS, W., SNELL, A. M., and BUTT, H. R. (1940), *Surg. Clin. N. Amer.*, **20**, 1005.

PREPENILE SCROTUM

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THIS is a report on an interesting anomaly of the external genitalia occurring in a male African of the Mwera tribe.

Embryology of the External Genitalia.—External genitalia in the course of their development pass through an indifferent stage before the definite sexual characters are recognizable.

A surface elevation called the genital tubercle appears in the midline just cephalic to the cloacal membrane. This genital tubercle lengthens, and along its caudal surface there appears a median groove which extends caudally towards the proctodeum. The urogenital sinus now opens into the floor of this median groove between the genital tubercle and the proctodeum. The margins of the median groove are known as the genital folds. On either side of the genital folds, and separated from them by distinct grooves, elevations known as the genital swellings appear. These are the forerunners of the labioscrotal folds.

In the male the genital tubercle becomes elongated to form the penis. The median groove on the caudal surface deepens owing to an increase in size of the genital folds, and these gradually begin to close over the median groove to form the penile urethra. The opening of the urogenital sinus is thus transferred to the end of the penis. The line of closure of the urethral groove is marked by the penile raphe.

The genital swellings situated on either side of the developing penis enlarge. This development progresses most markedly in their caudal portions, which expand and unite with each other in the midline on the anal side of the root of the penis. The scrotum is thus formed. *Fig.* 231 shows diagrammatically the sequence of events in the development of the male and female genitalia (Patten, 1947).

It is conceivable that if the region of greatest activity in the genital swelling occurred in an area cephalad to its usual site, the labioscrotal folds would unite on the umbilical side of the root of the penis and give rise to the anomaly described below. In the case described, however, the fusion of the labioscrotal folds has not been completed. A band of skin connects the two scrotal pouches.

CASE REPORT

An adult African, aged 40 years, and a carpenter by trade, was admitted to hospital on April 15, 1952, suffering from a right-sided pneumonia. Routine examination revealed the following described congenital anomaly of his genitalia.

A bifid scrotum hung down in front of a penis 6½ cm. in length. The median raphe extended from the anus to the end of the penis. The two scrotal pouches each contained a normal-sized testicle. A band of skin connected the fundus of each pouch, indicating the site at which fusion of the genital swellings had started but had failed to continue. The prepuce was missing and the patient said that he had been circumcised by the elders of his tribe when a boy. However, some redundant skin, the remains of the prepuce, was present inferiorly. This is the custom in African tribal circumcision here.

The external meatus and glans penis were normal, as also was micturition. An intravenous excretory pyelogram and cystogram revealed no other abnormality of the genito-urinary tract. Cystoscopy revealed no abnormality of the trigonal region.

The patient was married and had had one child, who died of malaria at the age of 3 years.

The congenital anomaly is shown in *Fig.* 232.

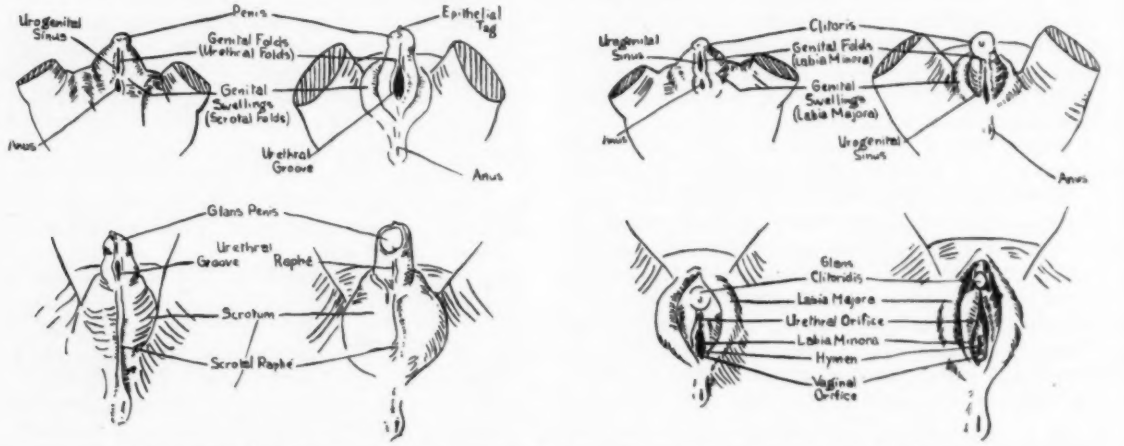


FIG. 231.—Showing the stages in development of the external genitalia in the male and in the female.

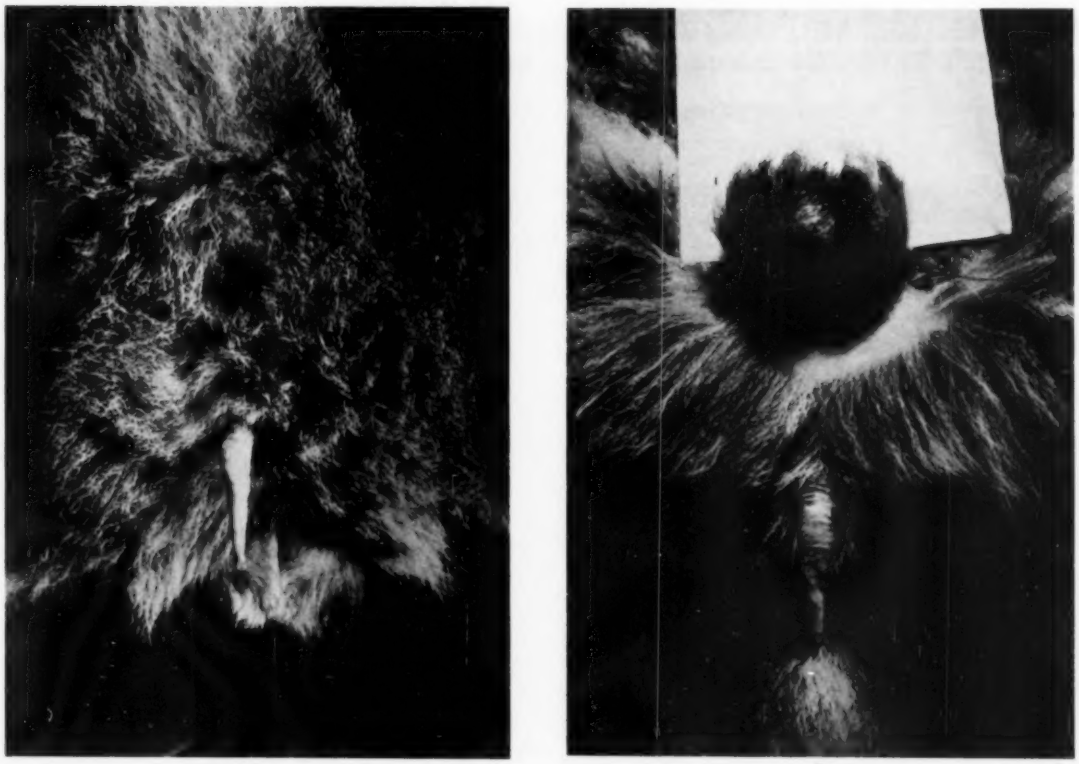
FIG. 232.—Showing the prepenile scrotum. The band of skin connecting the two scrotal pouches is obscured in A, but is well shown in B and C, in which it has been raised to show the dorsum of the penis.

COMMENT

A prepenile scrotum (*Fig.* 233) is a normal arrangement of the external genitalia in Marsupials. W. C. Osman Hill, Prosector of the Zoological Society of London, in a personal communication reports that the condition also occurs in the Tupaioids (tree shrews of Malaya), which are generally understood to be on an intermediate evolutionary level between the Marsupials and the Primates. In some lower Primates, like Tarsius, the testes tend to be parapenile, as if indicating a halfway stage between the prepenile and postpenile positions.

A search of the literature reveals records of only three similar cases, all of them in infants with other congenital abnormalities. This is the only case of an adult so far reported. L. F. Huffman (1951) described a case of a robust infant which lived nineteen days with congenital cystic kidney and the ureters opening ectopically into the bowel. In addition, the infant had a prepenile scrotum and the anomaly is described by him thus: "A rather large scrotum containing both testicles was situated anteriorly in the pubic region. Posterior to this was a pendulous penis 7 cm. in length. The median raphe extended from the anus to the tip of the penis and was absent over the scrotum. The meatus and glans penis appeared normal." (*Fig.* 234.)

Huffman in his article quotes from a case reported by C. C. Francis (1940). This infant lived only for forty-seven minutes and presented the following abnormalities: "The scrotum was large, had no median raphe, and was attached immediately above



A B

FIG. 233.—Photographs illustrating the prepenile scrotum in marsupials. These were taken from a freshly dead body of a Bennett's wallaby (*Macropus rufogrisea fruticus*). B is a photograph of the ventral aspect and A was taken from behind with the tail lifted up.

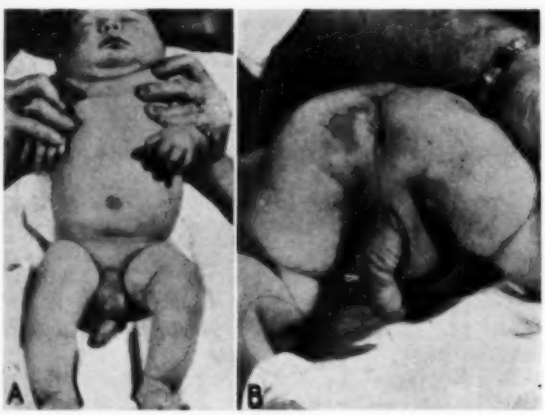


FIG. 234.—Shows the prepenile scrotum in the case described by L. F. Huffman.

the symphysis. The perineum was undeveloped so that creases over the adductor muscles met in the midline. The penis, placed about 3 cm. behind the scrotum, had a median ventral raphe and a rudimentary glans and prepuce. The navicular fossa was present in the glans, but there was no penile urethra. The anus was dorsally placed and the tip of the coccyx projected backwards as in the chimpanzee."

A third case, a patient of Professor Hildebrand, is referred to by Francis. This child was several months old and had a perineal hypospadias and a prepenial scrotum.

SUMMARY

1. A report is given of a curious congenital anomaly of the external genitalia occurring in an adult male African.

2. An account of the embryology of the external genitalia is included, with a note on the comparative anatomy and references to three other cases described.

I wish to thank the Director of Medical Services, Tanganyika, for permission to submit this article for publication.

Fig. 231 from *Human Embryology*, by Bradley M. Patten, are reproduced with the permission of the publishers, The Blakiston Company, Inc., New York.

Fig. 234, from the article by L. F. Huffman in the *Journal of Urology*, Vol. **65**, is reproduced by permission of the publishers, The Williams & Wilkins Company, Baltimore, U.S.A.

Fig. 233 was kindly sent to me by Dr. W. C. Osman Hill, M.D., Prosector of the Zoological Society of London.

REFERENCES

FRANCIS, C. C. (1940), *Anat. Rec.*, **76**, 303.
HUFFMAN, L. F. (1951), *J. Urol.*, **65**, 141.
JOHNSTON, T. B., and WHILLIS, J. (1938), 27th ed. *Gray's Anatomy*, 193.
PATTEN, BRADLEY M. (1947), *Human Embryology*, 600, 601.

THE LATE REPAIR OF CLEFT PALATE BY MAXILLARY OSTEOTOMY, WITH TUBE PEDICLE CLOSURE OF THE NASOBUCCAL FISTULA*

By PATRICK CLARKSON and W. G. GROSSMAN

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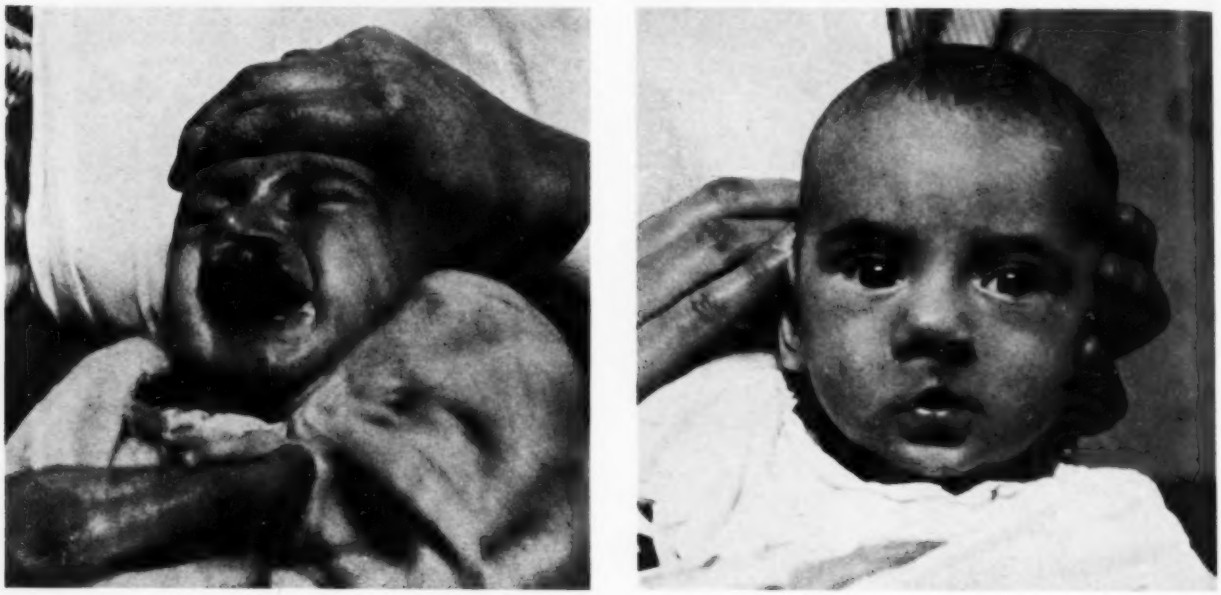
THIS is a report on the result of treatment for an orthodontic deformity and speech disability difficult to correct by other means. The methods described here were both introduced by Sir Harold Gillies. These are a reduction of the collapsed maxillary arch by osteotomy, and the closure of the enlarged palatal fistula by soft tissue transported from a distance as a tube pedicle.

There are some major clefts of the palate which we believe it is impossible to close from local tissue. There are many others in which a closure by local flaps is only obtained at the expense of a severe restriction of growth of the maxilla, particularly of the alveolar arch on the affected side. The late results in these cases are a gross malocclusion of the collapsed affected alveolar arch or arches, often associated with an open bite, and a diminution of the growth of the maxilla in all dimensions, which is reflected in the facial contour of the patient by flattening of the cheeks and a sinking of the upper lip. The collapse of the maxillary arcade is often so great that when the teeth on it are lost (and they often are at an early age) it may be impossible to construct a stable denture which will occlude with any mandibular teeth. In such major clefts the palate closure has commonly been under tension, and a palatal fistula of variable size is sometimes present and necessitates a prosthesis which, however good, cannot give a water-tight closure, needs removal for cleansing, is breakable, and has to be renewed from time to time.

The scarred hard palate and the soft palate, which is almost always short in all dimensions and rigid, produce a typical speech disability which in severer cases means that the patient is incomprehensible for most of the time. Every one of these patients has at least a detectable nasality of speech.

A reduction of the lower half of the maxilla by multiple osteotomies to bring the alveolar arch into occlusion with the mandibular teeth can only be done at the expense of considerable enlargement of the palatal fistula. This enlargement can be readily accepted if soft tissue in abundance, by tube pedicle from outside the mouth, is available to close it. Such tube pedicle tissue acts, as Gillies has pointed out, as a living obdurator. All hard palate mucosa posterior to the fistula can be displaced backwards into the soft palate to increase its antero-posterior diameter and consequently its efficiency in speech production. The whole of this enlarged soft palate can then be freed from the hard palate; this clearance is carried out well laterally to the region of the tuberosity on either side. An abundance of tube pedicle tissue is let in along the whole anterior surface of the soft palate and fixed to the margins of the hard palate fistula so that the backwards displacement of the soft palate is maintained.

Maxillary osteotomy is a major procedure, as is the operative stage of the attachment of the tube pedicle to the soft palate and the border of the hard



A B

FIG. 235. – A, Three-months-old baby with a major cleft of lip and palate and gross flattening of nostril. B, Primary repair of lip and floor of nostril by Sir Harold Gillies.

* Based on a paper read at the Annual Meeting of the British Association of Plastic Surgeons, Salisbury, September, 1953.

palate fistula. There are in addition a number of stages necessary in the preparation of the tube pedicle before its intra-oral attachment. Such a major and protracted programme of surgery can only be justified for patients with a marked disability, for those whose co-operation can be depended upon, and whose intellectual and economic state make the improvement worth while in terms of the demands which the treatment makes on the patient.

A B

FIG. 236.—A, B, The lip result and condition of the palate at about 5 years.

FIG. 237.—The lip at the age of 17 years. Notice the very reasonable symmetry of the nostril following the primary lip and nostril repair.

In the case described here the tube pedicle inset into the lip and mouth was combined with the stage of reduction of maxillary alveolus by osteotomy.

CASE HISTORY

This boy of 18 had been born with a major cleft of the left lip and palate. At three months old the lip cleft was closed by Sir Harold Gillies. Later in childhood two attempts by other surgeons of great experience and skill in this work had been made to close the palatal cleft. The fistula shown in *Fig.* 235 persisted. The soft palate was intact but short in its anteroposterior diameter. He spoke with a marked nasality of speech and when tired or under any emotional stress was virtually incomprehensible. He wore an obturator to cover the hard-palate fistula. There was collapse of the left maxillary arcade and gross mal occlusion (*Fig.* 237-239).

The plan adopted was to reduce the left maxilla by the Gillies maxillary osteotomy technique, and to repair the palate by tube pedicle tissue. The tube pedicle was raised from the tissues around the lower part of the neck. This site was chosen to avoid the need of an intermediate vector, and because donor scars in this situation are acceptable in some men. At the stage of the osteotomy the lip scar was opened, the left buccal sulcus incised throughout its extent, and the left anterior surface of the pyriform fossa and antrum exposed. The left hard palate in front and behind the fistula was divided in the midline. Chisels were then passed through the medial and anterior left antral walls just above the level of the floor of the antrum. An incomplete osteotomy through the posterior wall of the antrum and the maxillary tuberosity was then done at this level. The left maxillary alveolus could then be levered readily into proper occlusion, where it was fixed in its new relation to right maxillary alveolus and the the left mandible by locking bars screwed on previously cemented cast-metal splints. The right end of the ' necklace ' tube pedicle was divided, this end of the tube pedicle, dependent now on its left

pedicle, was swung up into the lip and alveolar part of the cleft, where it was sutured into position. The secondary neck defect was closed by approximation. Hexamethonium, by lowering the blood-pressure and reducing the bleeding produced by the osteotomy, which

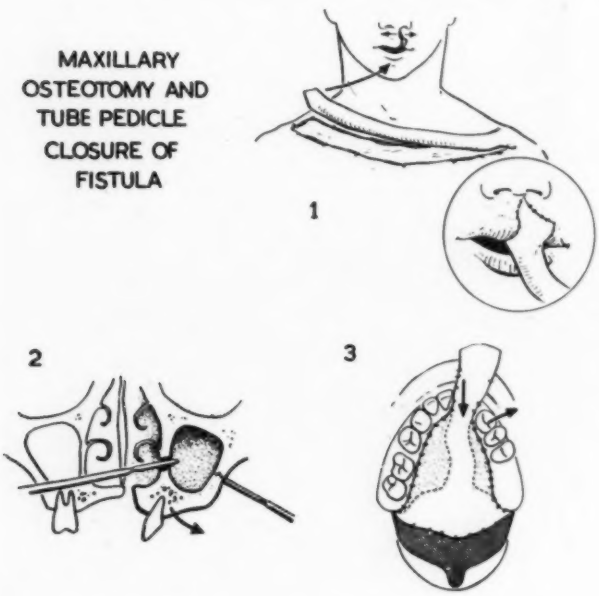


FIG. 238.—This diagram illustrates the plan of treatment adopted for this patient. The 'neckless' tube pedicle was attached to the re-opened left cleft and alveolus at the time of the osteotomy; the other end was later let in to the hard palate and anterior border of the soft palate to act as a living obturator after the soft palate had been displaced backwards.

lip was reclosed. The present appearance of the lip is acceptable but a revision of it and of the buccal sulcus is planned for the future.

TECHNIQUE OF DENTAL FIXATION.—Splinting and fixation of a case of maxillary osteotomy with tube pedicle differs from routine splinting.

The usual intermaxillary locking device cannot be used as the jaws must be kept open sufficiently to allow for the tube pedicle to lie between the upper and lower front teeth.

In the case described in this paper, the palatally displaced $\underline{5}|$ and a deformed $|\underline{1}$ were extracted pre-operatively. In the upper jaw, sectional silver-cap splints were cemented, the right section covering $\underline{7\text{–}1}|$ and left $|\underline{3\text{–}5}$. Both sections had locking plates over the buccal aspects of the premolars, whilst on the palatal aspect orthodontic locks of the Mershon type were fitted. The lower C.M. splints covered $\underline{7}|\underline{7}$. Locking plates were fixed to the buccal aspects of the splints in both pre-molar regions.

A 25-mm. opening in front was considered necessary to allow the tube pedicle to enter the oral cavity. Pre-operatively, a wax-bite was taken with the jaws open to this extent. With the help of this bite, an acrylic wedge was made which could be inserted between the occlusal surfaces of the right upper and lower premolars. It could be screwed to the locking plates on the upper and lower cap metal splints. A secure fixation on the right, resulting in an anterior opening of approximately 25 mm. was then obtained.

To enable an immediate fixation of the left maxillary fragment, following osteotomy, the fish plates of the left upper and lower jaw were joined by a 1½-mm. hard stainless-steel wire, shaped to a double-U loop (*Fig.* 242). The positive parts of the Mershon locks were also connected to each other with the help of a double-U loop 1½-mm. strong stainless-steel wire. After reduction of the left maxilla, the acrylic wedge was inserted and

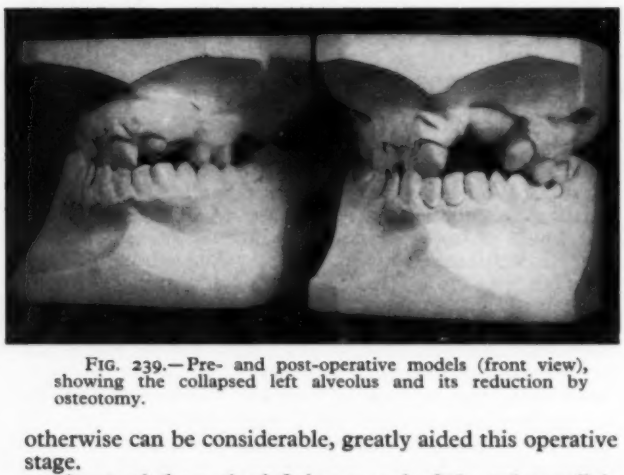


FIG. 239.—Pre- and post-operative models (front view), showing the collapsed left alveolus and its reduction by osteotomy.

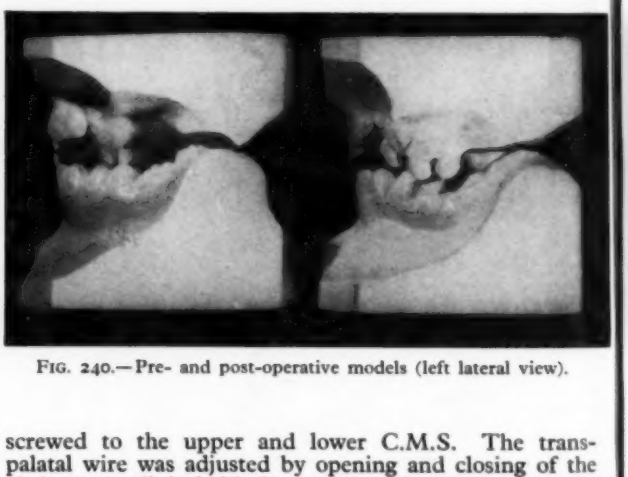


FIG. 240.—Pre- and post-operative models (left lateral view).

otherwise can be considerable, greatly aided this operative stage.

A month later the left lower end of the tube pedicle was divided. The hard palate mucosa was separated from the hard palate and displaced backwards with the soft palate, which was dissected from the posterior border of the hard palate as far laterally on each side as the region of the tuberosity. The soft palate could then be made to fall back on the posterior pharyngeal wall, leaving in front of it a very considerable fistula of the type that is seen in the Gillies-Fry operation. This fistula was closed by tube pedicle tissue hinging backwards from its anterior lip attachment. There was primary healing at this junction of soft palate and tube-pedicle.

At later stages the anterior part of the tube pedicle was let into the front of the hard palate and alveolus and the screwed to the upper and lower C.M.S. The trans-palatal wire was adjusted by opening and closing of the U loops until it held the mobile left fragment in the desired position. The intermaxillary fixation on the left was similarly adjusted and screwed into position. This was later replaced by a strong metal bar connecting both fish plates. The transpalatal wire, held by the Mershon lock, was kept until the second stage of the operative treatment.

The occlusion, post-operatively, was found to be satisfactory. The distance between the buccal cusps of $\underline{4}|\text{-}|\underline{4}$ which was 30 mm. pre-operatively, was found to be 40 mm. after treatment was completed. This means a lateral shift of the left maxilla of 1 cm. The previously completely inadequate space for $|\underline{1}\,\underline{2}$ can now be considered normal, allowing for a satisfactory prosthetic appliance.

RESULTS OF OPERATION.—The cast-metal splints fixing his jaws in proper occlusion were maintained for four months. In the year and a half since operation the union has remained solid and the correct occlusion has been maintained.

As the result of this operation the patient now has a water-tight and air-tight closure of his fistula by living tissue, and a correction of his mal-occlusion with a left upper alveolus to which an occluding denture could be fitted should he become edentulous. It is of particular interest to note that he has a very greatly improved speech. His effective nasopharyngeal closure is shown by his ability to whistle and blow up the cheeks. He has much improved vowel sounds. Although traces of nasality are still detectable, his speech is now comprehensible at all times.

FIG. 241.—Occlusal view of upper models, pre- and post-operative, showing the closure of the fistula by tube pedicle tissue, as well as the left alveolar reduction.

COMMENTS

A low neck tube pedicle was used for this male patient. The donor site for a woman is the abdomen, with the arm as the intermediate vector. This takes longer to prepare and transport to the palate, 3–6 months as against 2 months. When an oblique scar on the upper and exposed parts of the neck can be accepted, a tube pedicle from this region may be used and inserted into the mouth through an incision at the angle of the jaw, as described by Kitlowski of Baltimore. We prefer the low neck tube pedicle for men; but we also are strongly of the opinion that Gillies is right in teaching that when a tube pedicle is inserted into the palate it should be given, at that or an earlier stage, an intermediate attachment to the lip or to a cheek scar. If this is not done the whole weight of the pedicle drags on the skin-mucosal suture line, with the pedicle hanging down from the palate obstructing the oral cavity; feeding difficulties are increased, and separation of the pedicle-palate suture line is likely to occur.

We have always (in six cases) inserted the tube pedicle to the anterior border of the soft palate, without splitting the soft palate or prolonging the attachment of the tube pedicle backwards to the posterior wall of the nasopharynx, as we believe Gillies has done in selected cases. We have made no attempt to provide lining for the upper surface of this tube pedicle closure of the hard palate, which heals by granulation and ingrowth of nasal mucosa. The resultant upper contracture helps to reproduce the concavity of the palate, which is unavoidably absent in the early stages.

Although it would be perfectly practicable from the technical point of view to insert a tube pedicle which would close the palatal fistula at the time of the osteotomy, there are reasons for not doing this. The chief of these is that it would be impossible to strip the mucosa from the reduced alveolus and hard palate (as is done with advantage later) without danger to the main blood-supply of this fragment.

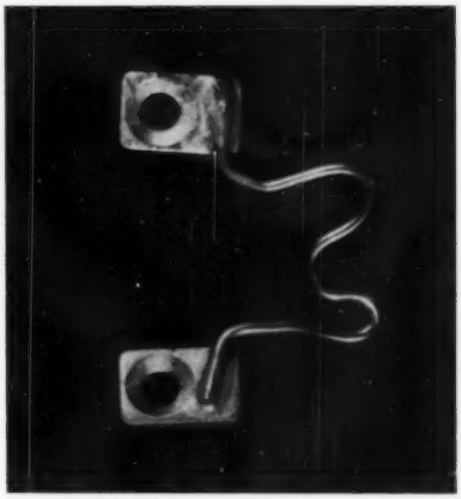


FIG. 242.—Fish plates connected by 1½-mm. stainless steel wire.

The osteotomy done for this patient was based on the technique taught at Basingstoke by Gillies for this condition. It was one in which a lateral shift only was needed to bring the left maxillary alveolus into correct occlusion. There was no open bite pre-operatively and no downward displacement of the left alveolus was necessary to close the bite on the affected side. When an open bite has to be corrected the angular gap in the tuberosity region which is established by this reduction should be packed with cancellous bone chips. If this bone-graft is not done in such cases a late recurrence of the open bite may occur.

The gap in the alveolar region was closed for this patient by tube pedicle soft tissue; it was not considered necessary to insert later a bone-graft to restore the alveolar ridge. This would have been perfectly practicable, and is done when the alveolar gap is a large one, and reconstruction of the bony alveolus will benefit the efficiency of dentures.

SUMMARY

The treatment of a case of old severe cleft lip and palate, with persistent fistula, gross malocclusion, and severe speech disability, by reduction of the maxillary alveolus by osteotomy and closure of the enlarged hard palate fistula by tube pedicle tissue, is described. This treatment, which was spread over nine months, has resulted in greatly improved speech, correction of the malocclusion, and closure of his fistula by living tissue.

This patient was treated throughout at the Plastic Unit, St. Charles's Hospital. It is a pleasure to record our appreciation of the constant help and advice which was afforded us there by Mr. Robin Dale, and of the skilled anæsthesia by Dr. Randell which so greatly facilitated the operations.

INTESTINAL OBSTRUCTION BY GALL-STONE

By W. J. FRASER

SENIOR REGISTRAR IN SURGERY, BURY AND ROSSENDALE HOSPITAL GROUP

THE condition is uncommon. Vick (1936) gives its incidence as 0·7 per cent of all cases of intestinal obstruction. Several series of cases have been previously reported. My reasons for reporting yet another are that the incidence and mortality-rates are so different from these other series; that in 2 cases exploration of the gall-bladder was carried out at a later date because of stones felt at the first operation; and that in several the diagnosis was suggested prior to operation. This last fact I attribute to seeing the first two cases and then being alive to the possibility of the others.

The series consists of 7 cases. The average age of the patient was 66 years, which is in the age group normally presenting the condition. The mortality was 2 cases out of 7, or 29 per cent. Most authorities give the mortality-rate as about 50 per cent. Six of the cases were operated on in Bury and 1 in Crewe. The 6 cases in Bury are included in 201 cases of acute intestinal obstruction which were operated on in the years 1948–52. This gives an incidence of 3 per cent of cases of acute intestinal obstruction, compared with the figure quoted above. No explanation of this rather high incidence can be given apart from the fact that chronic cholecystitis is a common disease in Lancashire.

CASE REPORTS

Case 1.—E. N., female, aged 65. Admitted on June 30, 1949 as a case of cholecystitis, having started to vomit more than usual. There had been previous attacks of pain in the epigastrium and right hypochondrium, for which investigation had been declined. The vomit on admission was not copious but consisted of gastric contents only. Within twenty-four hours it became copious and foul smelling. A barium meal was requested and showed grossly distended small bowel and a hold up of barium. After pre-operative gastric aspiration and intravenous fluids the abdomen was explored (W. R. D.). A large oval gall-stone was found in the upper ileum and was removed. Closure of the incision in the bowel so limited the lumen that a side-to-side anastomosis was required. The patient developed a paralytic ileus and auricular fibrillation and died on July 4.

Case 2.—F. C., female, aged 65. Admitted on April 18, 1950, with a five-day history of acute central abdominal colic and constipation. For the twenty-four hours before admission there was copious vomiting of fæcal smelling fluid. The abdomen was distended and borborygmi were present. The abdomen was explored (F. M. H.) and a large oval gall-stone was removed from the middle ileum. There was commencing ulceration at the site of impaction and this was invaginated by Lembert sutures. Pre- and post-operatively she received intravenous fluids and gastric suction. She made an uninterrupted recovery (not even a paralytic ileus!) and was discharged home on May 5.

Case 3.—B. C., female, aged 79. Admitted on Oct. 23, 1950, with a history of central abdominal colic and vomiting for three days. Constipation was also present. She had been treated with repeated enemata by her own doctor. On the second day a copious loose motion was obtained but the pains continued. On admission she was grossly dehydrated and was vomiting copious quantities of foul smelling brown fluid. The abdomen was distended, and though the patient was not at all clear in her own mind about time (owing to her distress), she said that about a day before admission the pain became much worse and remained constant with acute colic superimposed. She was seen by Mr. Morrison, who suggested the probability of the obstruction being due to gall-stone. After preliminary correction of dehydration and gastric suction the abdomen was explored (W. J. F.). A large oval stone was removed from the terminal ileum. As purulent free fluid was present a perforation was thought to be present also. On tracing the bowel upwards a small perforation was found in the ileum three feet from the point of impaction. This was closed by Lembert sutures. The abdomen was drained.

The day after operation her condition improved. She developed auricular fibrillation on Oct. 25. This was treated by digitalis. The intravenous fluids and gastric suction were maintained. On Oct. 27 the bowels opened spontaneously, but a fæcal fistula developed on Oct. 28. This was copious for two days and the patient appeared to be greatly improved. The bowels then began to open slightly and the fistula improved, but congestive cardiac failure developed and did not respond to treatment. She died on Nov. 11.

Case 4.—J. S., male, aged 64. Admitted on April 21, 1951, with a three-day history of severe central abdominal colic with vomiting, constipation, and distension. His own doctor had treated him " for his gall-bladder " some five years previously. A radiograph erect showed fluid levels to be present and operation was proceeded with (F. M. H.). A large oval gall-stone was removed from the ileum. Pre- and post-operative suction and intravenous fluids were given as usual. No paralytic ileus developed, but an infected hæmatoma of the wound discharged on May 5. Recovery thereafter was uneventful. He was discharged home on May 17 and when seen subsequently at the follow-up clinic was feeling " champion ". Even careful post-operative scrutiny of the X-ray films failed to reveal any radio opaque gall-stone.

Case 5.—J. H., female, aged 41. Admitted on May 22, 1951, with sudden onset of severe central abdominal colic ten hours before admission. The pain was accompanied by copious vomiting. Distension and borborygmi were present along with dehydration. There had been no previous operations and a pre-operative diagnosis of intestinal obstruction due either to gall-stone impaction or adhesion to mesenteric glands was made. The abdomen was explored (W. J. F.) and a large oval gall-stone removed from the terminal ileum. The gall-bladder was palpated and found to contain two smaller faceted stones. The patient made an uninterrupted recovery and was discharged on June 2.

At the follow-up clinic a cholecystogram showed a non-functioning gall-bladder but no opaque calculi. After discussion with colleagues it was decided to explore the gall-bladder. This was done on Feb. 9, 1952 (W. J. F.). It was found to be fibrosed (pencil-size) and empty. It was adherent to duodenum and transverse colon. No attempt to interfere with it was made. An uninterrupted recovery followed and when seen almost a year later she was feeling very well.

Case 6.—A. V., female, aged 65. Seen first at O.P. (W. M.) complaining of recurring upper abdominal colic with jaundice. A slightly tender mass could be felt in the right hypochondrium. The patient was obviously recovering from an attack of acute cholecystitis and investigation demonstrated a non-functioning gall-bladder with no opaque stones. Her name was put on the waiting list for cholecystectomy.

On June 9 she was admitted with a forty-eight hour history of central abdominal colic with vomiting of brown fluid and constipation. The abdomen was distended. Borborygmi and dehydration were present. A diagnosis of intestinal obstruction due to inpaction of gall-stone was made. Operation was proceeded with (W. J. F.) after correction of dehydration. A large oval gall-stone was removed from the lower ileum. The gall-bladder was palpated and found to contain several small stones. She made a rapid uninterrupted recovery. As with *Case* 5 it was decided to explore the gall-bladder and an exactly similar condition was found—a fibrosed empty organ adherent to duodenum and transverse colon. Nothing was done. When seen six months later she was very well.

Case 7.—M. H., female, aged 81. Admitted to Crewe Memorial Hospital on Aug. 10, 1952, complaining of abdominal colic for forty-eight hours, with vomiting of copious amounts of brown fluid for eight hours. Distension was present with borborygmi. She gave a history of flatulent dyspepsia and upper abdominal colic for many years. A diagnosis of gall-stone obstruction was made and after correction of dehydration and gastric suction an oval gall-stone was removed from the lower ileum (W. J. F.). The gall-bladder contained many small stones and was adherent to the duodenum by its fundus. She developed a mild paralytic ileus, but thereafter made a good recovery. She was very well when last I heard of her in February, 1953. No further exploration of the gall-bladder is contemplated.

DISCUSSION

Diagnosis.—The diagnosis is usually of acute small-bowel obstruction, except for the few cases where the stone impacts in the large bowel. Exact pre-operative diagnosis is really not essential. As Todd (1953) remarks, " diagnosis is not an end in itself but a means to providing treatment ". If one can diagnose the obstruction before gross vomiting occurs and while distension is minimal, then treatment can begin early and the prognosis is infinitely better. Every hour wasted increases the likelihood of paralytic ileus. Everyone advises operation with the least possible delay. How can one achieve this?

1. Liaison with the general practitioner is most important. One must try to discuss cases with the G.P. I think it is most unlikely that the practitioner who gave repeated enemata to *Case* 3 will do so again when confronted with a similar patient!

2. Extremely careful examination is imperative. One may have to wait several minutes before one sees a patient having an intestinal colic. One must also insist on the patient lying really flat or one misses slight distension, and auscultation of the abdomen must never be forgotten—the loud tinkling sounds are always present.

3. The greatest assistance is, however, given by radiography. Lloyd Williamson (1952) discusses this fairly fully. He quotes Rigler, Borman, and Noble (1941) and Nogaard (1942), who suggest a barium meal. In his opinion it is a grave risk both by making a partial obstruction complete and by delaying operation. I agree with this and feel there is little or no place for giving a barium meal to a patient suspected of having intestinal obstruction.

On the other hand a plain film with the patient erect is most valuable. It is not my practice to ask for one in an obvious case of small-bowel obstruction, but to have one in all cases of abdominal colic with no or only slight distension with increased bowel sounds. It is not essential to see many fluid levels before diagnosing intestinal obstruction. One or two levels with a few loops of distended gas-filled bowel are sufficient to indicate that obstruction is present and ought to be relieved. One must be careful, however, to ensure that no enema has been given prior to the radiograph being taken, as this will give a picture showing many fluid levels. The bowel, however, in this event will not be distended abnormally.

Having arrived at the diagnosis of acute small-bowel obstruction, one is free to speculate on its cause. The following two points should make one at least mention the possibility of it being due to a gall-stone: (1) A history of cholecystitis is suggestive but must often be sought for specifically. It was present in 4 of the 7 cases—an unusually high figure. (2) A history of intermittent obstruction is very suggestive, especially in association with (1), but is not diagnostic of gall-stone impaction. My most typical case of intermittent obstruction was caused by a fæcolith in the ileum. Only 1 of the 7 cases presented this feature.

It is unusual to see the obstructing gall-stone in the plain radiograph. In none of the cases in this series which were radiographed was it seen. This is because most stones are non-opaque and in any film where there is much distension and many fluid levels the faint shadow of an opaque stone is easily obscured.

Treatment.—Everyone advises operation as soon as possible. Dehydration must first be corrected and gastric suction instituted. Anæsthesia falls naturally under the jurisdiction of the anæsthetist, but my preference is for epidural xylocaine with adequate basal narcosis.

The stone once located is removed through a longitudinal incision in the bowel wall after applying occlusion clamps and packing off the area. The incision is sewn up transversely to minimize stenosis. It is essential to search proximally for any other stone which may be present and which one is certain to find if the one removed has a facet. The search may even reveal a perforation at the site of previous impaction. It is only complete when the ileum, jejunum, duodenum, stomach, and gall-bladder have been palpated. If any of the former four contain a stone it must be removed unless small. If the gall-bladder contains several stones it is reasonable to expect that they will be passed spontaneously and no further interference is indicated. If a large stone is felt in the gall-bladder it should be removed if possible, but one's actions must be governed by the patient's general condition at all times.

Post-operatively the gastric suction and intravenous administration of fluid is continued until there is little result from the former and the bowels begin to act naturally.

SUMMARY

Seven cases of small-bowel obstruction due to gall-stone impaction are recorded.

The incidence was 3 per cent of all cases of acute intestinal obstruction operated on during the years 1948–52.

The mortality-rate was 29 per cent, or 2 cases in 7.

The role of X rays in diagnosis is discussed.

Suggestions are made for treatment if further stones are found in the gall-bladder.

My thanks are due to Mr. W. R. Douglas, Mr. W. Morrison, and Mr. F. Mitchell-Heggs, under whose care the patients were admitted, for permission to publish the cases and for their help in diagnosis and treatment; to Dr. D. J. A. Brown and his registrars for excellent anæsthesia; to the various house surgeons for their maintenance of fluid balance; and lastly, but equally with all the others, to the nursing staff to whose efficient care these patients owe so much.

REFERENCES

Foss, H. L., and Summers, J. D. (1942), *Ann. Surg.*, **115**, 721.

Lee, M. (1945), *Brit. med. J.*, **1**, 555.

Nøgaard, F. (1942), *Acta radiol., Stockh.*, **23**, 622.

Rigler, L. G., Borman, C. N., and Noble, J. F. (1941), *J. Amer. med. Ass.*, **117**, 1753.

Todd, J. W. (1953), *Lancet*, **1**, 482.

Turner, G. Gray (1932), *Brit. J. Surg.*, **20**, 26.

Vick, R. (1936), *Maingot's Post-graduate Surgery*, **1**, 1017. London: Medical Publications Ltd.

Williamson, J. C. F. Lloyd (1952), *Brit. J. Surg.*, **39**, 339.

EXPERIMENTAL SURGERY

AN ANGIOGRAPHIC STUDY OF THE RENAL CIRCULATION IN EXPERIMENTAL HYPERTENSION IN THE DOG

By P. M. DANIEL, MARJORIE M. L. PRICHARD, and J. N. WARD-McQUAID*

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This angiographic study on dogs was a small parallel investigation undertaken in association with a much larger study on rabbits (Daniel, Prichard, and Ward-McQuaid, 1954, a). As in the work on rabbits, the object was to see whether there was any change in the renal circulation in experimental hypertension. It had been suggested by Trueta, Barclay, Daniel, Franklin, and Prichard (1947) that in this condition the blood-flow through the renal cortex might be diminished, while that through the medulla is well maintained or even increased.

METHODS

Young adult dogs, weighing from 6·5 kg. to 13 kg., and including both sexes, were operated upon with aseptic precautions. Pentobarbitone anæsthesia was used for the determination of the blood-pressure level before the application of the clamp, for right nephrectomy, and for angiography. Sodium pentothal anæsthesia was used when intermediate blood-pressure readings were taken (by percutaneous puncture of the femoral artery with a needle connected to a mercury manometer). When the normal blood-urea and blood-pressure levels had been ascertained the right kidney was excised intraperitoneally through an abdominal incision. A week or a fortnight later the left kidney and its pedicle were exposed extraperitoneally through an oblique muscle-cutting loin incision. A Goldblatt clamp (Goldblatt, 1940, 1948) was then applied either to the main renal artery itself or to its primary anterior or posterior division. The gap between the two plates of the clamp was decreased (from its maximum of 2 mm.) by 0·5 mm. with each complete turn of the screw, the degree of constriction applied varying with the size of the dog. After application of the clamp the kidney was exteriorized between the loosely approximated muscles of the loin and the skin. The levels of the blood-pressure and the blood-urea were then determined at various intervals.

For angiography a polythene catheter was inserted into the femoral artery, and when the femoral arterial pressure had been measured the catheter was passed up into the aorta to the level of the renal artery. The animal was placed on its back with the exteriorized kidney lying over the film aperture (5 × 6 in.) of the serial angiographic apparatus, and an injection of thorotrast (a contrast medium which is not excreted by the kidney) was made through the catheter. The amount of thorotrast injected varied from 7 to 20 ml., according to the size of the dog. The passage of the contrast medium through the kidney was recorded on 18 serial X-ray films, exposed at rates of 2 per second for the first 12 films and 1 per second for the remaining films. The duration of each exposure was 0·05 sec.

The kidney and the clamped renal artery were then exposed and the pressures in the artery on each side of the clamp were measured, a serum needle connected to a mercury or capacitance manometer being inserted into the artery, first distal to the clamp and subsequently proximal to it. In two animals the form of the pulse wave in the artery on each side of the clamp was recorded. When the pressures had been taken, the animals were killed and a post-mortem examination was made. The kidneys of some dogs were injected post mortem with 2 per cent Berlin blue (in distilled water).

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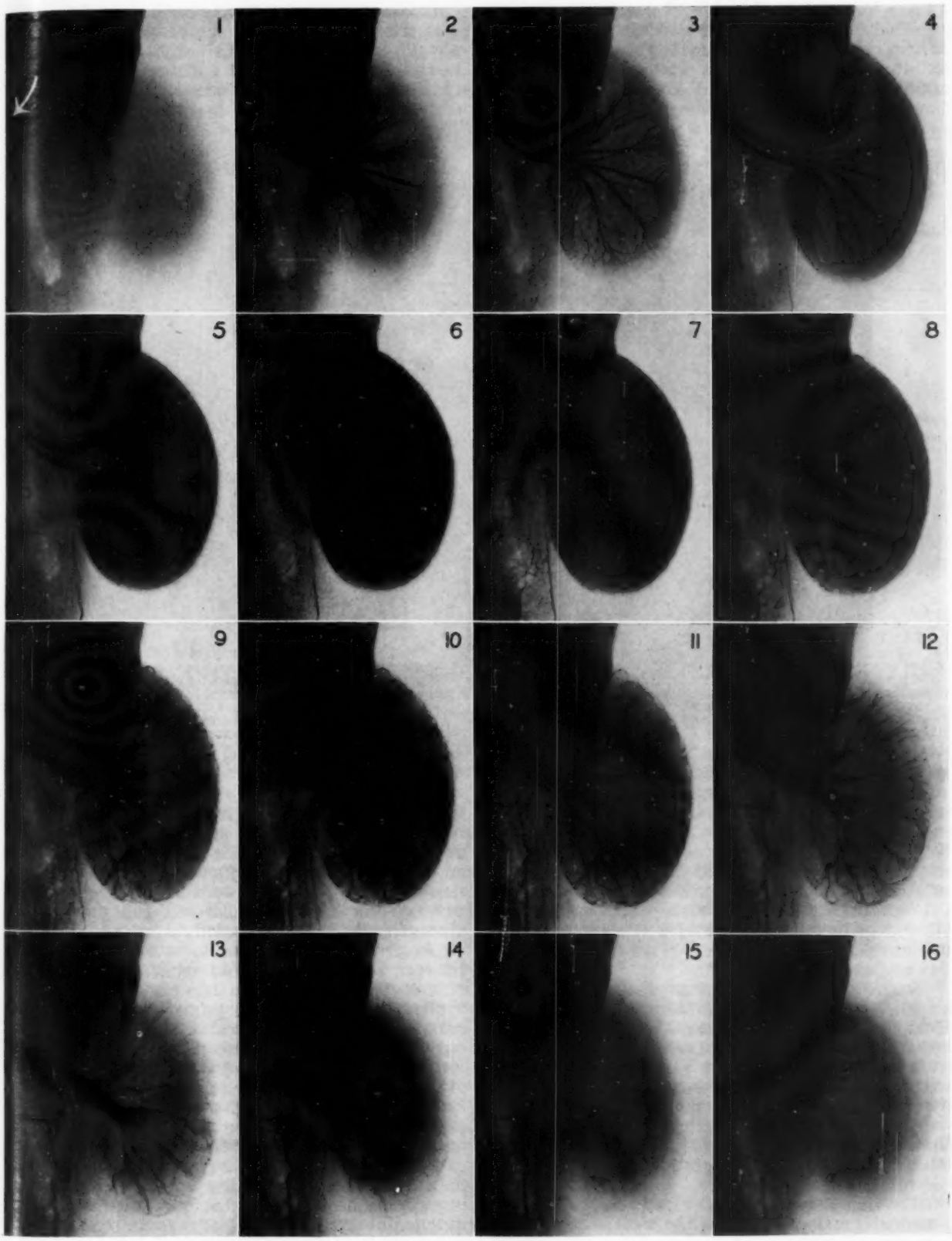

FIG. 243.—Serial angiograms showing the circulation through the exteriorized kidney of a dog, to illustrate the type of record on which observations were made. Nos. 1-12 were exposed at a rate of 2 per sec., and Nos. 12-16 at 1 per sec. A Goldblatt clamp (partly seen at arrow in No. 1) had been placed on the main renal artery ten days previously, but the dog had not become hypertensive. The picture of the renal circulation is normal. Note that the cortex is best seen in the late arterial and early capillary phase of the circulation, and the medulla in the venous stage. The renal vein is first visible in No. 7, and well seen in No. 8.

RESULTS

There was a good deal of variation in the response to the constriction of the main renal artery in the 17 dogs which made a satisfactory recovery from application of the clamp. Nearly all the animals, however, had a rise of blood-pressure. Some dogs suffered from fits and died from hypertensive uræmia after a few days, but the others remained in good health, although two became uræmic later, one of these going blind.

FIG. 244.—Angiogram taken from a serial record showing late arterial and early capillary phase in a dog with 'benign' hypertension. The clamp (not visible) had been in position on the main renal artery for ten days, and the systemic blood-pressure had risen 30 mm. Hg above the pre-operative resting level. Compare with *Fig.* 245, and note the good perfusion of the kidney.

Constriction of one of the two primary branches of the renal artery produced hypertension in 7 out of 9 dogs. In 2 of these animals the hypertension did not persist for more than four weeks. Two other dogs of this group developed a severe degree of nitrogen retention, with blood-urea levels of 256 and 496 mg. per 100 ml.

Angiograms.—Angiograms were made on 6 animals, from 8 to 21 days after application of a Goldblatt clamp to the main renal artery. The gap between the plates of the adjusted clamp varied from 1·5 to 1·875 mm. In 1 animal there was no sustained rise of blood-pressure, but in the others the rise was from 20 to 45 mm. Hg above the normal, pre-operative level. The blood-urea levels of 4 animals were within normal limits, but in the other 2 they were 154 mg. per 100 ml. and 500 mg. per 100 ml.

The animal with no rise of blood-pressure showed a normal renal circulation (*Fig.* 243) with a good perfusion of both cortex and medulla and a renal circulation time of 2·5 seconds. The angiographic picture and the time relations of the passage of the contrast medium through the cortical and medullary circulations were remarkably similar to those seen in normal dogs (Daniel, Peabody, and Prichard, 1951). Three of the animals whose blood-pressure had risen also showed an apparently normal renal circulation (*Fig.* 244). However, in the animal with a blood-urea level of 500 mg. per 100 ml., and which we regarded as having 'malignant' hypertension, the renal circulation was greatly diminished (*Fig.* 245), both the cortex and the medulla being affected, and the circulation time (3·5 sec.) being longer than normal. The dog with a blood-urea level of 154 mg. per 100 ml. showed similar but less pronounced changes in the renal circulation.

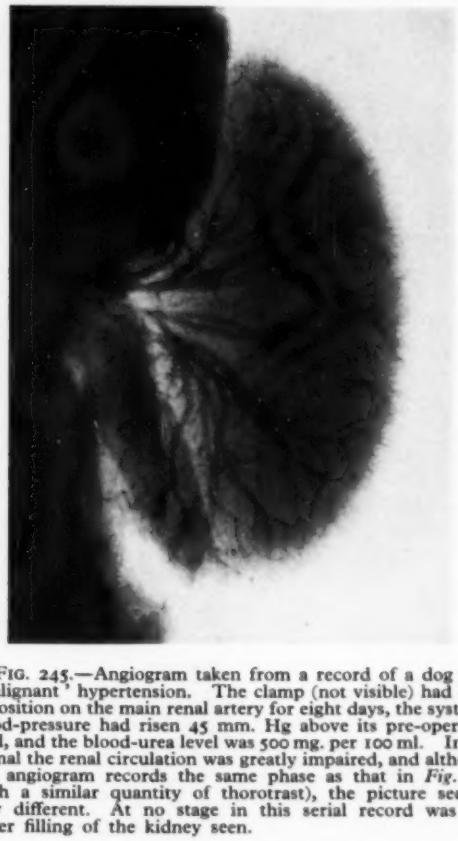

FIG. 245.—Angiogram taken from a record of a dog with 'malignant' hypertension. The clamp (not visible) had been in position on the main renal artery for eight days, the systemic blood-pressure had risen 45 mm. Hg above its pre-operative level, and the blood-urea level was 500 mg. per 100 ml. In this animal the renal circulation was greatly impaired, and although this angiogram records the same phase as that in *Fig.* 244 (with a similar quantity of thorotrast), the picture seen is very different. At no stage in this serial record was any better filling of the kidney seen.

Angiograms were also made on 6 further animals between 10 and 42 days after application of a Goldblatt clamp. In 5 of these dogs the clamp had been applied to one of the two primary branches of the renal artery, and in 1 animal it had been placed on one of the two, more or less equal-sized, renal arteries found to be present. The gap between the plates of the adjusted clamp varied from 0·625 to 0·75 mm. Four of these animals had a rise of blood-pressure of 30 to 40 mm. Hg above their normal levels, but in the other 2 the pressure had fallen to normal and to 20 mm. Hg above normal respectively by the time the angiograms were made. In all these animals the circulation through that part of the kidney supplied by the 'clamped' artery was reduced; in some instances it was virtually absent. At post-mortem examination this part of the kidney was in most animals found to be atrophied or even infarcted. In the part of the kidney supplied by the artery

without a clamp no circulatory abnormality was seen, except in the one animal whose blood-urea level was raised (256 mg. per 100 ml.). This dog showed in the 'unclamped' part of the kidney a reduced perfusion, a patchy cortical ischæmia, and a circulation time longer than normal (3·5 sec.).

Blood-pressure on Each Side of the Clamp.—In 7 animals the blood-pressure in the renal artery on either side of the Goldblatt clamp was determined, without any fall in the systemic blood-pressure having occurred as a result of the operative exposure. In 5 dogs in which the clamp was on the main renal artery, the drop in mean pressure varied from 15 mm. to 50 mm. Hg. These values included a pressure drop of 22 mm. Hg recorded in the dog whose systemic blood-pressure had returned to normal by the time the angiograms were made.

In 2 animals the pressures were measured on either side of the tighter clamp placed on one of the two primary branches of the renal artery. In these the mean pressure drop across the clamp was 14 and 44 mm. Hg. The reduction in the pulse wave and the change in its form in the first of these dogs is shown in *Fig.* 246.

Berlin Blue Injections.—In the four kidneys injected with Berlin blue no abnormality was seen, in the distribution of the mass either in the 'clamped' or 'unclamped' parts of the kidney. The blue was found in glomeruli throughout the cortex, as well as in the vessels of the medulla, even in those parts of the kidney which had become atrophic.

DISCUSSION

Exteriorization ('explanting') of the kidney, which made it possible to obtain renal angiograms of good definition with minimal disturbance of the animal, did not appear to affect the general health of the dog, its renal circulation, or systemic blood-pressure. This had also been found to be the case in the experiments on rabbits (Daniel and others, 1954, a).

In our hypertensive dogs the drop in mean pressure across the clamp, when this was applied to the main renal artery, ranged from 15 mm. to 50 mm. Hg, compared with a pressure drop of 40–60 mm. Hg found by Trueta (1950) in greyhounds. Levy, Light, and Blalock (1938) found that in their hypertensive dogs the pressure in the renal artery distal to the clamp was 38–50 mm. Hg lower than the pressure in the femoral artery, whereas in normal dogs the pressure in the renal artery is generally somewhat higher than that in the femoral artery. In rabbits with chronic 'benign' hypertension we had observed a mean pressure drop varying from 3 mm. to 20 mm. Hg across a clip placed on the renal artery. In those dogs in which a tighter clamp was applied to one of the primary branches of the renal artery the drop in pressure across the clamp was not found to be greater than that observed in the dogs whose main renal artery had been constricted.

A reduction in the pulse wave beyond the clamp was also noted in our dogs. This is of interest in view of the opinion expressed by Page and Corcoran (1948) that a reduction of the intrarenal pulse pressure is the 'trigger mechanism' in initiating experimental renal hypertension. In only one of our dogs did we examine histologically the renal artery at the site of the clamp, but this showed some loss of elastic tissue, a feature which had been prominent in our rabbits with clip hypertension (Daniel, Prichard, and Ward-McQuaid, 1954, a, b). It seems possible that a loss of elasticity of the wall

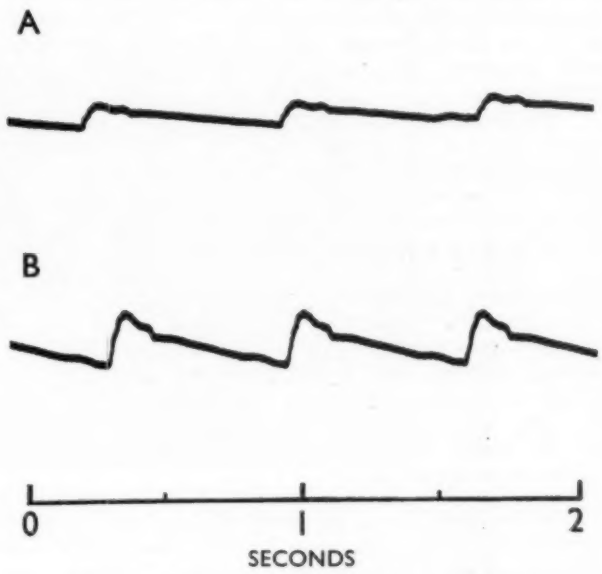

FIG. 246.—Pulse-wave distal (A), and proximal (B) to a clamp on one of the two primary divisions of the renal artery (recorded by capacitance manometer). Pressures: A, 126/112; B, 151/115.

of the renal artery may be a factor of some significance in the development of this type of experimental hypertension.

Angiographically, the only animals which showed any abnormality were those which had developed uræmia. In these the circulation through both the cortex and the medulla was noticeably impaired. In all the other dogs no obvious change could be detected in the renal circulation either in the kidney as a whole when the clamp was on the main renal artery, or in the unclamped part of the kidney when the clamp was on one branch of this artery. In the latter case, however, the circulation through the 'clamped' part of the kidney was greatly diminished or even absent.

The period during which angiograms were made was limited to 2–6 weeks after application of the clamp, but in so far as these experiments on dogs correspond with those on rabbits (Daniel and others, 1954, a) the results obtained were similar. In the rabbits, in the first week after application of a renal artery clip (a time when no angiograms were made on the dogs) there was a general reduction in the renal circulation. No obvious changes could be seen in the angiograms of rabbits with 'benign' hypertension of moderate or long duration, although in rabbits which developed 'malignant' hypertension the renal circulation was severely impaired.

Thus this series of 12 dogs and the much larger group of rabbits (Daniel and others, 1954, a) provided no evidence of a substantial change in the

relative distribution of the intrarenal blood-flow between the cortex and the medulla. These findings agree with the normal renal clearances which have been reported in dogs with experimental hypertension by several authors (Smith, 1951).

SUMMARY

Dogs, after a right nephrectomy, were made hypertensive by the application of a Goldblatt clamp either to the left renal artery itself or to one of its two primary branches, the left kidney being exteriorized.

Rapid serial angiograms of the renal circulation were made of 12 dogs, from 8 to 42 days after application of the clamp. When the constriction had been applied to one branch only of the renal artery the circulation through the 'clamped' part of the kidney was greatly diminished. The circulation through the remaining 'unclamped' part of the kidney, and through the whole of the kidney in dogs with a clamp on the main renal artery, showed no obvious abnormality, except in a few animals which developed uræmia; in these the renal circulation as a whole was impaired.

The pressures in the renal artery on either side of the clamp were measured and the form of the pulse wave recorded.

The experiments reported in this paper were carried out at the Buckston Browne Research Farm, Downe, Kent, and at the Nuffield Institute for Medical Research, Oxford.

Our thanks are due to Dr. H. Goldblatt for sending us one of his clamps to serve as a model for those used, which were made for us by Mr. A. Lord, Department of Hæmatology, Radcliffe Infirmary, Oxford.

We also gratefully acknowledge the technical assistance of Mr. R. Mason and Mr. F. Watson at the Buckston Browne Research Farm; and of Mr. M. S. Tuckey at the Nuffield Institute for Medical Research.

REFERENCES

DANIEL, P. M., PEABODY, C. N., and PRICHARD, M. M. L. (1951), *Quart. J. exp. Physiol.*, **36**, 199.

— — PRICHARD, M. M. L., and WARD-MCQUAID, J. N. (1954 a), *Brit. J. Surg.*, **42**, 81.

— — — — — — (1954 b), *Quart. J. exp. Physiol.* **39**, 81.

GOLDBLATT, H. (1940), *Amer. J. clin. Path.*, **10**, 40.

— — (1948), *The Renal Origin of Hypertension.* Springfield, Ill.: C. C. Thomas.

LEVY, S. E., LIGHT, R. A., and BLALOCK, A. (1938), *Amer. J. Physiol.*, **122**, 38.

PAGE, I. H., and CORCORAN, A. C. (1948), *Experimental Renal Hypertension.* Springfield, Ill.: C. C. Thomas.

SMITH, H. W. (1951), *The Kidney.* New York: Oxford University Press.

TRUETA, J. (1950), *Glasg. med. J.*, **31**, 217.

— — BARCLAY, A. E., DANIEL, P. M., FRANKLIN, K. J., and PRICHARD, M. M. L. (1947), *Studies of the Renal Circulation.* Oxford: Blackwell Scientific Publications.

SHORT NOTES OF RARE OR OBSCURE CASES

COMPRESSION OF THE TRACHEA BY AN ABNORMAL INNOMINATE ARTERY

By VICTOR S. BROOKES

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ABNORMAL arrangements of the great vessels at the root of the neck or in the upper mediastinum are occasionally met with and may present difficulties in diagnosis and treatment. In most of the recorded cases the condition appears to have superficially resembled an aneurysm of one of the great vessels, and pressure effects on the trachea and/or œsophagus have usually been evident. The following case is a further example of such abnormalities and is interesting in that it presented as a 'goitre'.

CASE REPORT

The patient, a woman, was first admitted under the care of the Birmingham Surgical Professorial Unit, in 1947 when she was 50 years of age. She had been aware of a swelling in the neck for twenty years, but this had caused no symptoms until three years before admission. Then she began to get dyspnœa and palpitations on exertion, a feeling of suffocation when she lay flat, and huskiness of the voice. Shortly before admission she had an attack of laryngitis. At the onset of her symptoms her own doctor had given her iodine by mouth for six months, but this had had no effect on the swelling in the neck. Although she appeared very apprehensive she showed no evidence of thyrotoxicosis. The radial pulse-rate was 70 per minute, but she also had many extrasystoles. Blood-pressure was 135/70 mm. Hg. The swelling in the neck appeared to be in the thyroid gland and chiefly in its left lobe, the trachea being displaced to the right of the midline. A diagnosis of adenomatous enlargement of the left lobe of the thyroid was made and operation was undertaken. The operation note made at that time said that the left lobe of the thyroid was enlarged and it was almost completely removed. The right lobe was said to be normal. The convalescence was uneventful.

The patient returned to hospital in September, 1953, with a further swelling in the neck and said that she still had all the symptoms originally complained of. She undoubtedly had a prominent swelling in the neck which appeared to be in the right lobe of the thyroid gland. Again there was no evidence of thyrotoxicity. The pulse at the wrist was 50 per minute, but the apex beat was 84 per minute and there were many extrasystoles. E.C.G.

showed the extrasystoles to be ventricular in origin, but apart from them the E.C.G. was normal. It was thought that the patient had further adenomatous enlargement of the thyroid gland and further operation was advised.

AT OPERATION (Sept. 24, 1953).—The old skin incision was re-opened and the infrahyoid muscles separated vertically in the midline. It then became obvious that the swelling in the neck was a normal right lobe of the thyroid which was being displaced forwards on to the front of the trachea. The left lobe of the thyroid was of course almost completely absent. It was observed that the trachea was still displaced to the *right*, and that this displacement was due to a second swelling lying in front of the trachea and below the lower pole of the thyroid right lobe. This swelling which lay above the suprasternal notch was pulsating. Further dissection was carried out and it was found that the swelling consisted of the innominate artery. The arch of the aorta from which it arose extended upwards as high as the level of the suprasternal notch, and the point at which the innominate artery originated from the arch was much farther to the left than usual. This resulted in the artery running almost transversely from left to right, and it crossed the trachea at the level of the third to sixth tracheal cartilages. The displacement of the trachea was due to the artery and the trachea was also narrowed by its pressure. Immediately to the right of the trachea the innominate divided into right subclavian and right common carotid arteries. The latter, as it curved around the right border of the trachea and then up the neck, was responsible for the anterior displacement of the right lobe of the thyroid. The left common carotid artery appeared normal except that its origin from the arch of the aorta was also more to the left than normal. There was no major abnormal vessel to be felt or seen behind the trachea or œsophagus. None of the major vessels appeared to be aneurysmal. (*Fig.* 247.)

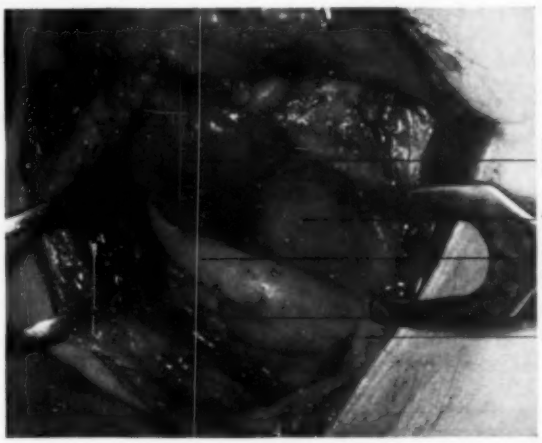

FIG. 247.—Photograph taken at operation showing the innominate artery lying across the front of the upper trachea and the displacement upwards and forwards of the right lobe of the thyroid by the common carotid artery.

In view of the patient's age it was considered unwise to divide the innominate artery. The separation of the infrahyoid muscles had allowed the artery to become displaced forward to a certain degree and seemed to relieve some of the pressure on the trachea. The muscles therefore were not sutured again. The platysma and skin were repaired.

Bronchoscopy performed at the end of the operation showed visible narrowing of the trachea about 1½ in. below the vocal cords.

During the dissection of the adventitious tissue around the innominate artery the pulse-rate rose quite suddenly by between 20 and 30 beats per minute and the extrasystoles became much less evident. This state continued for about 24 hours after operation, but then the pulse-rate again became slower, extrasystoles again became frequent, and the apex beat settled at about 85-90 per minute.

Post-operative X-ray screening of the chest showed no evidence of aneurysm in the major vessels and the radiographic appearances of the heart were normal.

DISCUSSION

The normal aortic arch is derived from the persistence of the artery of the fourth left branchial arch, and the normal innominate from the persistence of that of the fourth right branchial arch, while the subclavian arteries are almost entirely segmental in origin. By postulating variations in the ways in which the aortæ and the branchial arteries remain patent or become obliterated, many theoretical variations in the great vessels could be described. However, the variations seen often fall into a few well-defined groups, and these have been well classified by Gross and Ware (1946). In several of these types the abnormalities of the vessels may produce pressure on the trachea and/or œsophagus and give rise to dyspnœa or dysphagia. Beavan and Fatti (1947) recorded a case of abnormality of the great vessels in which almost a mirror image of the normal arrangement of the vessels was present. The arch of the aorta had arisen from the fourth right branchial arch. It passed in front of the trachea, then curved around its right border, passed behind the œsophagus to the left, and then descended as a normal, left, descending aorta. The arch of the aorta thus formed was abnormally high and was really in the neck. By forming an almost complete vascular ring around the trachea and œsophagus it had led to dyspnœa and dysphagia. They mistook the arch of the aorta for an aneurysm of the innominate or carotid artery and tied it, with fatal results. They were able to collect 12 similar cases from the literature, all with the same result. Lewis and Lambert Rogers (1953) recently recorded a similar case in which they fortunately realized the true state of affairs. In another type the pressure on the trachea and œsophagus may be caused by a vascular ring consisting of a double aorta, or be due to the presence of an abnormal right subclavian artery passing behind the œsophagus. d'Abreu, Astley, and Parkes (1952) recently recorded one of the latter type treated successfully by ligation and division of the artery behind the œsophagus.

In the case recorded here it would be easy to explain the high left arch of the aorta by presuming that the arch was due to the persistence of the third or even second branchial artery instead of the normally persisting fourth artery. One could not, however, satisfactorily explain on these embryological grounds the transverse lie of the innominate artery.

It has already been stated that no evidence of aneurysm or cardiac abnormality was found to explain the high position of the vessels.

If such an arrangement of the vessels were seen in a young patient and the symptoms were sufficiently serious, one could presumably divide the innominate artery if a temporary trial compression produced no cerebral ill effects.

I should like to thank Professor F. A. R. Stammers for his permission to publish this case.

REFERENCES

BEAVAN, T. E. D., and FATTI, L. (1947), *Brit. J. Surg.*, **34**, 414.
d'ABREU, A. L., ASTLEY, R., and PARKES, A. (1952), *Ibid.*, **40**, 70.
GROSS, R. E., and WARE, P. F. (1946), *Surg. Gynec. Obstet.*, **83**, 435.
LEWIS, C., and ROGERS, LAMBERT (1953), *Lancet*, **2**, 825.

SHRAPNEL BILIARY CALCULUS

A CASE REPORT

BY J. L. CONNELL AND S. B. ROSALKI
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THE following is a report of a case of obstructive jaundice due to the lodgment of a metallic foreign body in the common bile-duct. The rarity of this occurrence; the great length of time which elapsed between the injury and symptoms; and the distance between the site of the injury and final position of the foreign body in the common bile-duct, make this, we believe, a case worthy of report.

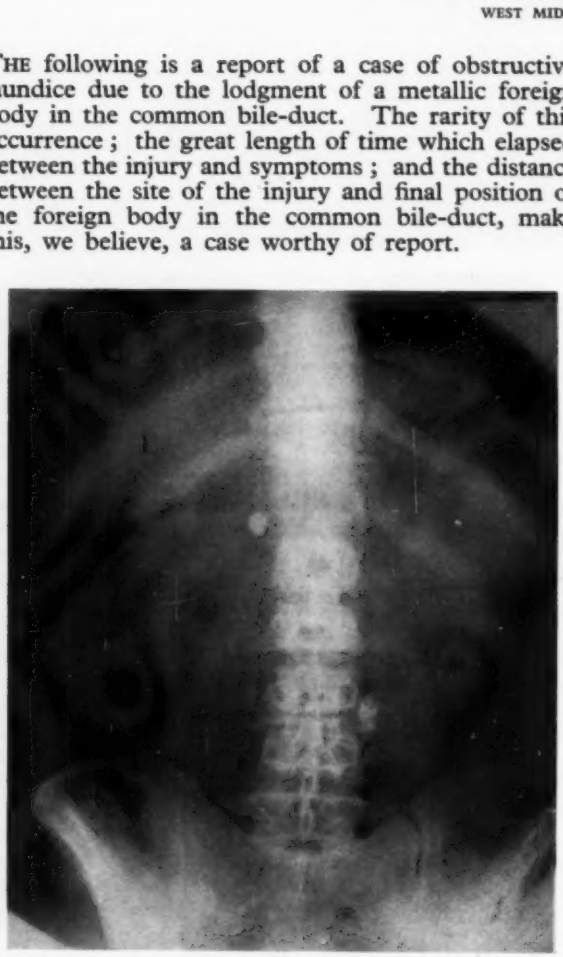

FIG. 248.—Radiograph showing opacity on the right side of the twelfth thoracic vertebra.

FIG. 249.—Post-operative choledochogram—the shrapnel visible in *Fig.* 248 has been removed.

CASE REPORT

The patient, Mr. F. H. R., a clerk aged 60, first attended Medical Out-patients in October, 1950, with a history of having had colicky epigastric pain six weeks previously. This pain persisted intermittently for three days, and ten days after its disappearance the patient noticed that his skin had become yellow, his stools pale, and his urine dark brown.

At the time of his examination in Out-patients he was no longer jaundiced, nor were any physical signs demonstrable, save the presence of three scars—one at the back of his right shoulder, and one on either foot, the three being relics of shrapnel wounds received at Ypres in 1914. It was thought that his jaundice had been obstructive in type, and laboratory investigations supported this view, the serum-alkaline phosphatase being raised (41·7 King-Armstrong units), whilst the thymol flocculation and serum-colloidal gold reactions were negative and the thymol turbidity normal (1 unit).

A plain radiograph of the abdomen failed to reveal any gall-stones, but a homogeneous opacity was visible on the right side of the twelfth thoracic vertebra (*Fig.* 248) and this was thought to be due to shrapnel penetrating into the abdomen at the time of the injury previously mentioned. A cholecystogram showed a normally filling gall-bladder with no stones visible.

Subsequent to his Out-patient visit the patient remained well for three weeks and then had a further attack of colicky epigastric pain lasting some hours and

followed the next day by jaundice. He was jaundiced when seen in Out-patients and was admitted the following week for investigation.

Investigations once more supported the presence of obstructive jaundice, but failed to reveal the nature of the obstruction. Whilst it was thought probable that the two attacks of jaundice were caused by biliary calculi, surgery was considered inadvisable owing to the failure of cholecystography to demonstrate evidence of biliary tract disease.

The patient was well and no longer jaundiced on his discharge from hospital a fortnight after admission. Nothing more was heard of him until he returned to Medical Out-patients in August, 1953, with a history of two recent attacks of colicky epigastric pain radiating to the right hypochondrium, both attacks being followed by jaundice. There was now little doubt that his attacks of jaundice and colic were due to gall-stones, and the following month he was admitted to a surgical ward for cholecystectomy and exploration of the common bile-duct.

AT OPERATION.—The gall-bladder was normal, but a large stone was palpable at the lower end of the common bile-duct. The entire gall-bladder area was free of adhesions, and the biliary tract was normal except for the presence of the stone. Cholecystectomy and choledocholithotomy were carried out, with T-tube drainage of the common bile-duct and drainage of the gall-bladder bed.

On subsequent examination the 'stone' removed from the common bile-duct was found to consist of a cube of jagged metal approximately 1 cm. × 1 cm. × 1 cm. in size, and surrounded by a coagulum of bile-pigment. This was obviously the piece of shrapnel noticed in the radiographs of 1952, and subsequent post-operative radiographs of the abdomen, performed during choledochography, showed that the shrapnel seen in the previous radiographs had indeed been removed (*Fig.* 249).

The patient's recovery from operation was uneventful, and he was fit and well on discharge.

DISCUSSION

Except for the scars of his operation, the patient had only three scars visible on his body: one on either foot and one small puckered scar 1 cm. across situated at the back of his right shoulder 8 cm. below the tip of the acromion process of the scapula—all three scars resulting from shrapnel wounds received at Ypres in 1914. It is assumed that the point of entry of the shrapnel removed from the common bile-duct was the wound on the right shoulder—this wound was followed at the time by pneumonia and so was not then explored. It is postulated that the piece of shrapnel entered the shoulder and the chest, penetrated the diaphragm, and lodged in the liver. It is thought that it then worked its way slowly and silently down the hepatic ducts—finally to lodge in the common bile-duct and give rise to symptoms thirty-eight years after the original injury. This is borne out by the absence of any history of wounding or cutaneous scarring, other than in the right shoulder and in the feet; and by the absence of abdominal symptoms following injury, and of any adhesions in the gall-bladder area, making it highly unlikely that the foreign-body entered the peritoneal cavity at the time of injury. It must, therefore, have entered the common bile-duct via the liver.

It is of interest to note that one previous case of 'shrapnel biliary calculus' has been described (Hurt, 1947), in which a mortar fragment ½ × ¼ × ¼ in., entering the right lower chest and known to have lodged in the liver at the time of injury, after giving rise to upper abdominal pain and clay-coloured stools, was removed from the common bile-duct six months after the original injury. In this case jaundice was absent, but it was noticed that coincident with the abdominal pain and clay stools, the flow of bile issuing from an external biliary fistula, which had developed from the injury, was increased.

SUMMARY

A case is described of recurrent attacks of biliary colic with jaundice, due to obstruction of the common bile-duct by a piece of shrapnel measuring approximately 1 × 1 × 1 cm. The shrapnel is thought to have penetrated the chest and entered the liver at the time of wounding in 1914, and to have worked its way slowly down the hepatic ducts to enter and cause obstruction of the common bile-duct some thirty-eight years after the original injury.

We wish to thank Mr. W. J. Ferguson for permission to publish this case.

REFERENCE

HURT, R. L. (1947), *Brit. J. Surg.*, **34**, 429.

A CASE OF BILATERAL TESTICULAR TUMOURS

SEMINOMA OF ONE TESTIS WITH TERATOMA IN THE OTHER

BY P. N. COLEMAN

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AND K. C. McKEOWN

SENIOR CONSULTANT SURGEON, DARLINGTON MEMORIAL HOSPITAL AND FRIARAGE HOSPITAL, NORTHALLERTON

THOUGH not common, the occurrence of bilateral tumours of the testes has been reported on a number of occasions. The literature is reviewed by Lewis and Priestley (1938) and Willis (1948), and single case reports include those by Peirson (1932), Grevillius (1937), Parker (1938), and Graves and Lawrence (1942). The tumours reported have most frequently been bilateral seminomas, but cases of bilateral teratomas have also been described. The case which is the subject of the present report is of interest because the bilateral tumours which occurred in the testes were of dissimilar types, one being a seminoma and the other a teratoma. We have not been able to find a similar case in the literature.

CASE REPORT

The patient, T. H. B., aged 30 years, had been married for two years and was the father of a child aged seven months.

In August, 1952, he noticed a swelling in the right testicle which was painless, but caused a dragging sensation in the right groin. The swelling persisted for some

FIG. 250.—Tumour of right testicle (*natural size*).

weeks, but subsequently retrogressed until January, 1953, when there was a progressive increase in the size of the swelling. One month later a swelling developed in the left testicle and the patient became aware of some diminution in sexual potency. There had been no injury to either testes and no history of previous genito-urinary infection.

ON EXAMINATION (April 1).—The patient was a well-nourished healthy looking man not unduly obese, and showing no signs of excessive mammary development. The right testis was the size of an orange, its surface was lobulated, and its consistency firm. The testis felt heavy and the epididymis could not readily be identified. There was no thickening of the spermatic cord and no fixity of the tumour to the scrotum. The left testis was not grossly enlarged, but was of stony hard consistency and insensitive to pressure. The epididymis was easily palpable, the cord normal, and the prostate not enlarged. The Wassermann reaction was negative, radiography of chest clear, and the Hogben test negative.

AT OPERATION (April 12).—The right testis was exposed, the diagnosis of testicular neoplasm confirmed, and the testis together with the spermatic cord excised. The scrotal septum was incised and the left testis delivered for inspection. The testicular tissue was largely replaced by a lobulated cartilagenous tumour, portions of which were taken for microscopy. Section showed the appearance of a chondroma.

The implications of further operation were explained to the patient, who decided, after some delay, to submit to removal of the remaining testis ; this being carried out on July 17.

DESCRIPTION OF TUMOUR.—The larger right-sided tumour (*Fig.* 250) measured 8 × 4 cm. and was of a uniform grey-white colour. Histological examination showed the typical appearance of seminoma (*Fig.* 251). There were clumps of rounded polyhedral cells each with a single spherical nucleus surrounded by a rim of palely staining cytoplasm separated by a stroma of connective tissue and blood-vessels. Sections were taken from all parts of the tumour and all showed the typical histological picture. The tumour from the left side (*Fig.* 252) occupied about two-thirds of the testis and was a sphere 3·5 cm.

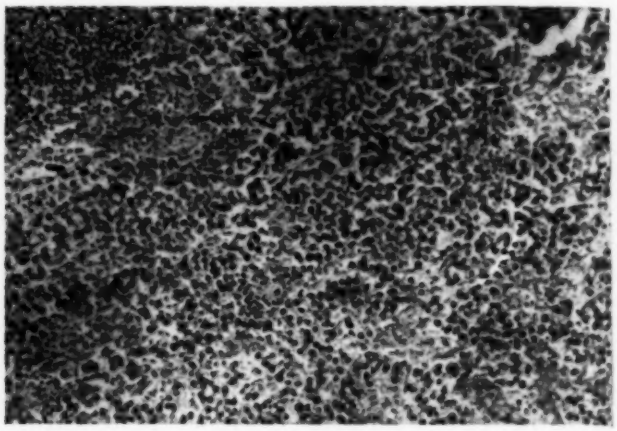

FIG. 251.—Photomicrograph of right tumour, showing appearance typical of seminoma.

in diameter. The tumour was a teratoma consisting largely of well-differentiated cartilage, but elements of bone, smooth muscle, and squamous epithelium could be made out. The structure of the whole of the tumour was surveyed, but no area resembling a seminoma was found (*Fig.* 253).

DISCUSSION

The case has an interest beyond the rare occurrence of bilateral testicular tumours of dissimilar types, since it has relevance to the problem of the relationship of seminoma to teratoma. There have been a number of reports of the coexistence of seminoma and teratoma, though in previous cases the tumours have occurred together in one testis. Ewing regarded the occasional coexistence of the tumours as evidence in favour of his view that seminoma was a one-sided development of a teratoma and always developed from a teratomatous precursor.

The problem has been reviewed by Willis (1948). He concluded that the association of seminoma with teratoma had been encountered too frequently to be fortuitous, but was unable to accept Ewing's hypothesis of the origin of seminoma. If the coexistence of the tumours is to support Ewing's hypothesis it must be shown that the seminomas had arisen from the teratomas, and in the examples he quoted Ewing considered that this had in fact occurred. Willis showed, however, that both in the cases quoted by Ewing and in other reported cases it was more probable that two separate and distinct tumours had arisen. In the present case there can be no argument on the fact that there were two tumours which had separate origins.

Having discounted the theory that a seminoma arises from a teratoma, Willis speculates as to the reason for the occasional association. He points out that seminoma frequently arose in a developmentally

abnormal testis. A teratomatous testis is developmentally abnormal and therefore perhaps predisposed to the occurrence of seminoma in the remaining testicular tissue. This cannot be the explanation in the present case. Another possibility suggested is that the teratoma might secrete some hormone-like substance which would influence the development of seminoma. The teratoma in the present case was not, however, of a type likely to secrete hormones, and tests for gonadotrophic hormones in the urine were consistently negative.

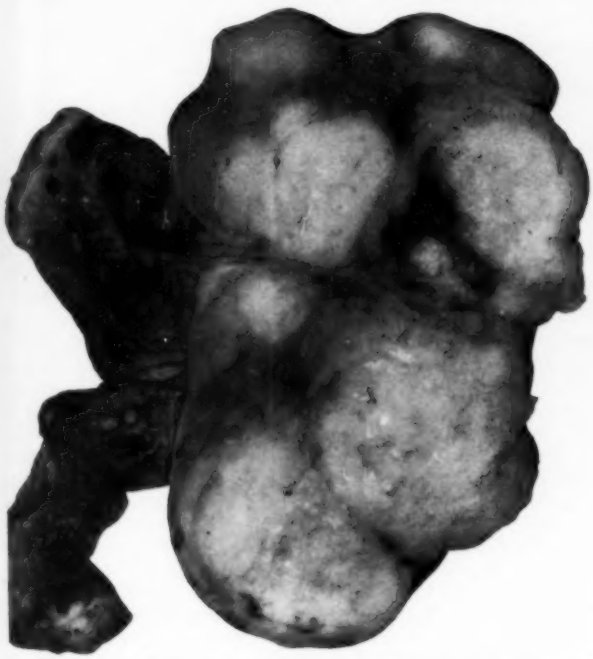

FIG. 252.—Tumour of left testicle. Macroscopically the tumour appears to consist almost entirely of cartilage.

There remains the tendency for testicular tumours to be bilateral. Willis quotes the opinion of Hamilton and Gilbert (1942), who from a review of the literature concluded that in a man with testicular cancer the likelihood of cancer arising in the second testis is a hundred times greater than the chance expectation. There appears to be no reason why the type of the tumour arising in the opposite testes should be the same as that of the original tumour.

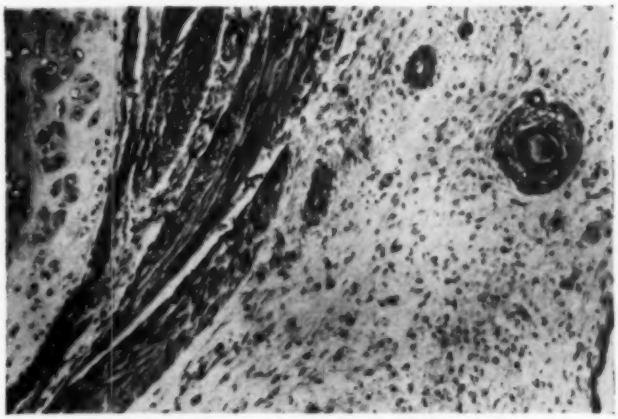

FIG. 253.—Photomicrograph of left tumour—a selected field which shows in addition to cartilage, smooth muscle, and a cell nest of squamous epithelium.

We wish especially to thank Professor R. A. Willis, who has examined the specimens and has given much help and advice.

Our thanks are also due to Mr. W. R. Hollingsworth, chief pathological technician, for the photography, and to Dr. R. Adamson, of Leyburn, for referring the case.

REFERENCES

GRAVES, R. C., and LAWRENCE, K. B. (1942), *J. Urol.*, **47**, 482.

GREVILLIUS, A. (1937), *Acta. chir. scand.*, Supp. 48, **79**, 1.

HAMILTON, J. B., and GILBERT, J. (1942), *Cancer Res.*, **2**, 125.

LEWIS, E. B., and PRIESTLEY, J. T. (1938), *Proc. Mayo Clin.*, **13**, 737.

PARKER, G. (1938), *Trans. med. Soc. Lond.*, **61**, 115.

PEIRSON, E. L., jun. (1932), *J. Urol.*, **28**, 353.

WILLIS, R. A. (1948), *Pathology of Tumours*. London: Butterworth.

WINSBURY-WHITE, H. P. (1948), *Textbook of Genito-Urinary Surgery*. Edinburgh: Livingstone.

REVIEWS AND NOTICES OF BOOKS

Textbook of Operative Gynæcology. By WILFRED SHAW, M.A. (Camb.), M.D., F.R.C.S. (Eng.), F.R.C.O.G., Late Surgeon in Charge, Gynæcological and Obstetrical Department, St. Bartholomew's Hospital; etc. 11 × 8½ in. Pp. 444 + viii, with 382 illustrations. 1954. Edinburgh: E. & S. Livingstone. £5.

IT is stimulating and indeed refreshing to read such a book as the one Wilfred Shaw has written, for it contains a wealth of surgical common sense and surgical detail. Although the book deals with operative gynæcology, yet it covers a number of non-gynæcological conditions such as appendicectomy, entero-anastomosis, and excision of colonic growths. This is all to the good, for in our opinion anyone who opens an abdomen should be competent to deal with any condition which may be discovered. It is tragic in these days to hear so often of patients who were operated upon for this or that and the abdomen closed because the operator considered a specialist should do the operation because he discovered the lesion was not his line of country. The gynæcologist who on opening the abdomen finds a non-gynæcological condition and closes the abdomen and hands the patient over to the general surgeon is not worth his salt. Why should the general public be subjected to such treatment?

The author of this splendid work was trained as a general surgeon and then he specialized in gynæcology. Surely this is the one and only way for gynæcological surgeons to be trained.

One of the great features of this book is the wealth of excellent illustrations, and Leslie Caswell is to be congratulated on his high standard of drawings.

Good illustrations enhance the value of any text-book, and the 382 drawings which illustrate this volume could not be bettered.

A great work of which British surgeons and gynæcologists may well be proud.

Fluid Balance in Surgical Practice. By L. P. LE QUESNE, M.A., B.M., B.Ch. (Oxon.), F.R.C.S. (Eng.), Assistant Director, Department of Surgical Studies, Middlesex Hospital. 8½ × 5½ in. Pp. 130 + viii, with 41 illustrations. 1954. London: Lloyd-Luke (Medical Books) Ltd. 17s. 6d.

THIS monograph represents the Moynihan Prize Essay for 1953, the prize awarded by the Association of Surgeons of Great Britain and Ireland. The author and winner of the prize is to be congratulated on an important piece of surgical research work. To-day surgeons have come to realize the importance of fluid balance in the pre- and post-operative treatment of their patients. With the increase in magnitude of many surgical operations the physiological needs of the patient must be maintained.

This book is written with a practical clinical background for the author describes in detail the various metabolic changes and the electrolyte balance that may occur in clinical surgery. The different forms of treatment necessary are fully discussed.

A useful book for the student, house surgeon, and registrar.

Historical Review of British Obstetrics and Gynæcology. 1800-1950. Edited by J. M. MUNRO KERR, R. W. JOHNSTONE, and MILES H. PHILLIPS. 9¾ × 7¼ in. Pp. 420 + viii. 1954. Edinburgh: E. & S. Livingstone Ltd. 30s.

THE editors of this large volume are to be congratulated on a very interesting historical work. The contributors come from the ranks of Senior Fellows of the Royal College of Obstetrics and Gynæcology and have given their services as a gift to their College on its Semi-Jubilee.

Medical historians will be grateful to the editors for the book is written as a sequel to H. R. Spencer's *History of British Midwifery* 1650-1800, which consisted of the Fitzpatrick Lectures, which were delivered in 1927.

The volume is divided into some thirty-eight chapters which in themselves cover a wide field, dealing with the Maternity Services and the rise of surgical gynæcology. The progress of radiotherapy in gynæcology and the sex hormones are also fully discussed.

An excellent production.

Anatomy for Surgeons. Vol. I. By W. HENRY HOLLINSHEAD, Ph.D., Professor of Anatomy, Mayo Foundation, University of Minnesota; Head of the Section of Anatomy, Mayo Clinic, Rochester, Minnesota. 10½ × 7 in. Pp. 560 + xii, with 326 illustrations. 1954. London: Cassell & Co. Ltd. 90s.

HOW does a book on Anatomy for Surgeons differ from any other anatomy book? Well, Professor Hollinshead has set out to demonstrate in the written word and in diagrammatic form those anatomical facts and concepts he considers will be useful to the surgeon. Professor Hollinshead's background as a teacher of anatomy to undergraduates for many years, and his matured practical experience at the Mayo Foundation, have fitted him well for this task.

The whole book is full of practical facts which are not stressed and not even mentioned in many books on anatomy. Also the vast number of original illustrations should prove of real value to the practising surgeon. These illustrations are excellent, for the author has been content to reveal the important structures and has entirely eliminated minute details.

The illustrations are purely diagrammatic and are planned to accompany the text, and the author is to be congratulated on an excellent production.

We look forward to seeing future numbers of this work.

Basic Anatomy. By G. A. S. MITCHELL, O.B.E., T.D., M.B., Ch.M., D.Sc., Professor of Anatomy and Director of the Anatomical Laboratories in the University of Manchester; and E. L. PATTERSON, M.D., Ch.B., B.Sc., Senior Lecturer in Anatomy in the University of Manchester. 9¾ × 6¾ in. Pp. 438 + viii, with 286 illustrations. 1954. Edinburgh: E. & S. Livingstone Ltd. 45s.

WHILE there seems to be a plethora of books on anatomy yet there is always room for one more if it provides something of value, and this text-book on Basic Anatomy certainly does that.

Professor Mitchell and Doctor Patterson tell us that this book is based on the introductory course of lectures given to the medical and dental students at Manchester University. The book certainly covers a wide field and is written in an interesting way, and the illustrations are excellent and many of them are original.

Students will find this book a grand basis on which to build their knowledge of anatomy, and lecturers will find much to interest them and something which will form a framework for their lectures.

The combination of straightforward fundamental anatomy, microscopic anatomy, and X-ray pictures is just what is wanted for an introduction to medical, dental, and physiotherapy students and this book covers all these in an excellent manner.

An Introduction to Pathology. By G. PAYLING WRIGHT, D.M., F.R.C.P., Professor of Pathology, Guy's Hospital Medical School, University of London. Second edition. 8⅛ × 5⅞ in. Pp. 636 + xii, with numerous illustrations. 1954. London: Longmans Green & Co. Ltd. 40s.

THE second edition of this useful and interesting text-book has been very thoroughly revised and will prove as popular with the student population as the first edition.

Professor Payling Wright's physiological interest and background have enabled him to write a book which will appeal to medical students for he has been able to cover in an admirable fashion the hinterland which lies between physiology and pathology.

Pathology is a difficult subject for students unless they are given the basic groundwork which can be found in such a book as this.

The illustrations throughout the book are excellent, especially the photomicrographs.

Medical students of to-day would be far happier in their studies if they had more books of this calibre within their reach and their pocket.

Clinical Orthopædics. No. 3. Edited by ANTHONY F. DE PALMA. 10 × 7 in. Pp. 230 + viii, with 139 illustrations. 1954. London: J. B. Lippincott Co. 60s.

THE third volume of this new series is devoted to soft-tissue conditions around joints. It contains some excellent articles by distinguished authors who are specialists in their own subjects. The treatment of sprains, and injuries to ligaments around joints, cysts of semilunar

cartilages, and dislocations of the patella are some of the outstanding chapters.

The second part of the volume is devoted to general orthopædics and contains articles on giant-cell tumour of bone, a clinical study of autogenous and frozen homogeneous bone in grafting operations, fatigue fractures, and fractures of the femoral neck.

This volume is full of practical information which is not to be found in books on orthopædic surgery, and it is interesting and refreshing to read this up-to-date contribution to surgery.

Spinal Epidural Analgesia. By P. R. BROMAGE, M.B., B.S. (Lond.), F.F.A.R.C.S., D.A., Consulting Anæsthetist, Chichester Hospitals Group; etc. 8½ × 5½ in. Pp. 123 + viii, with 41 illustrations. 1954. Edinburgh: E. & S. Livingstone. 15s.

THIS excellent monograph is especially welcome at the present time because the introduction of the muscle-relaxant drugs has largely tended to replace this method and it is valuable for the younger generation of anæsthetists to have available a full description of this technique.

The author informs us that the book is based on the records of 1000 cases carried out during the last five years, and it is interesting to note that the incidence of failure does not exceed 1 to 1½ per cent. Dr. Bromage states that in his opinion the standardized technique he describes has special advantages over other methods in producing ideal conditions for abdominal surgery and in certain therapeutic uses, and in our opinion he fully justifies his views on this subject. One of the great difficulties in attaining a high percentage of successes from this technique is the identification of the epidural space, and the author is to be congratulated on the admirable chapter he has so clearly written on this subject.

This book is excellently arranged and produced, and the illustrations deserve a special word of praise.

We recommend this book to all post-graduates preparing for the diplomas in anæsthesia.

Cleft Palate and Speech. By MURIEL E. MORLEY, B.Sc., F.C.S.T., Speech Therapist to the Royal Victoria Infirmary, The Hospital for Sick Children, and the Newcastle General Hospital, Newcastle-upon-Tyne. Third edition. 7¼ × 4⅞ in. Pp. 173 + xx, with 64 illustrations, some coloured. 1954. Edinburgh: E. & S. Livingstone Ltd. 17s. 6d.

THIS book is perhaps the best available work on an extremely complicated and difficult subject. The author's task is made more difficult than it might have been by the unfortunate fact that the nasopharyngeal sphincter, with the action of which her book is concerned, is not described in any of the standard text-books on which the medical profession and its auxiliaries are educated. The subject of this important mechanism has slipped unnoticed through the curious gap that exists between the anatomists who study the formation of the human body, and the physiologists who study its working. Miss Morley makes a gallant and interesting attempt to make good this gap with a description and figures of the action of the muscles, and follows this with a summary of the various operations recorded in the literature. This part of the book is unavoidably sketchy; but when describing her own work of speech training the author is admirably clear and full. She discusses with balanced judgement the limitations as well as the powers of her methods, and describes the many physical, psychological, and social difficulties that those who use them must expect to encounter.

Perhaps more discussion might have been given to the selection of those children, fortunately becoming more and more common, who will speak normally after operation without any training whatever; and also to the danger of producing grimacing and nervous tics by intensive drilling in movements of the face and throat.

In the case histories given it is striking to observe how few of these children have had the optimum surgical treatment, that is to say, who have had early and efficient closure of lip and palate clefts by a single surgeon used to this work. It is to be hoped that the work of such experts as Miss Morley will in the future be less and less handicapped in this way.

Problems in the Anatomy of the Pelvis. An Atlas. By UDUARD UHLENHUTH, Ph.D. 10 × 7 in. Pp. 206, with 82 illustrations. 1953. Philadelphia and London: J. B. Lippincott Co. 80s.

AT a time when the scope and complexity of surgical operations are increasing through the improvement in modern methods of anæsthesia and the control of adverse influences, the importance of a detailed knowledge of anatomy becomes daily more important to the surgeon. This book presents such a detailed study of the anatomy of the pelvis and it is concerned mainly with the controversial and difficult points which confront the practising surgeon.

It is in three sections: The first deals with the retrovesical space in the male; it covers all the anatomical difficulties concerned in such operations as total cystectomy and perineal prostatectomy. The fascial planes and ligaments of the bladder and the capsules of the prostate attain a new significance and their surgical importance can be appreciated.

The second deals with the musculature of the bladder and its sphincters and gives a reasonable interpretation of function as related to structure of this viscus. All the previous explanations are fully discussed.

The third covers the anatomy of the pelvic diaphragm and is not confined to the male.

The whole is illustrated by admirable large-scale drawings of numerous dissections.

Although there is much of purely academic interest in the work, we can commend it to the studious surgeon who wishes to base and improve his technique on sound anatomical principles.

Stone in the Urinary Tract. By H. P. WINSBURY-WHITE, M.B., Ch.B. (Edin.), F.R.C.S. (Eng. and Edin.), Senior Surgeon, St. Peter's Hospital and St. Paul's Hospital for Urological Diseases, London, etc. Second edition. 9½ × 6⅝ in. Pp. 342 + x, with 144 illustrations. 1954. London: Butterworth & Co. (Publishers) Ltd. 63s.

URINARY calculus is such a widespread and crippling disease that it merits serious study. In this second edition of his well-known work Mr. Winsbury-White has drawn upon his personal experience of a vast number of cases to give an account of the subject which is at once interesting and informative.

After an opening chapter on Aetiology and one on Composition, the remaining subject-matter is arranged on an anatomical basis, and despite the many recurring features of stone throughout the urinary tract the author has managed to avoid the repetition which sometimes follows this arrangement. The chapter on aetiology lays bare our fundamental ignorance of the ultimate cause of stone. The various possibilities are discussed at length, but there is the honest admission that we do not know all the contributory factors. This is one of the best chapters in the book, and one of the most comprehensible accounts of a difficult subject. It includes references to the literature up to 1949, and is, in fact, almost the only chapter which refers to papers later than 1940 or 1941. This is perhaps surprising in a

book published in 1954, but it again emphasizes the personal nature of the opinions expressed.

Not everyone will agree with all the recommendations; second-stage operations for diverticulectomy with stone are often even more difficult than single-stage procedures; the account of the various incisions for exposure of the kidney does not include that through the bed of the excised twelfth rib, nor indeed any of the more modern exposures. The inclusion of a coloured plate of a coexisting stone and 'hypernephroma' in the kidney suggests that the one caused the other, and this is stated in the text; emphasis on the causal relationship of stone and squamous carcinoma of the renal pelvis would have given a truer picture of accepted views.

The author is to be congratulated on writing a book which contains so much of practical value to the surgeon, and the publishers on producing it in their well-known attractive style.

Surgical Urology (Handbook of Operative Surgery). By R. H. FLOCKS and DAVID CULP. 8¼ × 5½ in. Pp. 392, with 118 plates. 1954. Chicago: Year Book Publishers (London: Interscience Publishers Ltd.). 73s.

THIS is a handbook of operative urology profusely illustrated by lucid drawings of the procedures described. Each section is introduced by an account of the anatomy and physiology of the region concerned and the whole forms a volume which will prove to be of great service to all who practise this branch of surgery.

There are very few omissions; the section on transurethral prostatic resection is confined to the McCarthy loop method, and some would prefer to see a description of the punch technique in place of some of the six methods of nephropexy which are included.

The clarity of the illustrations is a prominent feature of the book.

BOOK NOTICES

[*The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.*]

La Petite Chirurgie des Fistules Anales. By JEAN ARNOUS and ERNEST PARNAUD. 9¾ × 6¾ in. Pp. 134, with 17 illustrations and 5 colour plates. 1954. Paris: Masson et Cie. 1000 fr.

Experimental Surgery. By J. MARKOWITZ, M.B.E., M.B. (Tor.), Ph.D., M.S. in Exp. Surg. (Minn.). 9 × 6 in. Pp. 852 + xiii, with 554 illustrations. 1954. London: Baillière, Tindall, & Cox Ltd. 76s. 6d.

The Anatomy of the Bronchial Tree. With Special Reference to the Surgery of Lung Abscess. By R. C. BROCK, M.S. (Lond.), F.R.C.S. (Eng.), F.A.C.S., Thoracic Surgeon to Guy's Hospital; Surgeon to the Brompton Hospital. Second edition. 9⅜ × 6⅛ in. Pp. 243 + viii, with 157 illustrations. 1954. London: Oxford University Press. 45s.

Anatomy, Regional and Applied. By R. J. LAST, M.B., B.S. (Adel.), F.R.C.S., Professor of Applied Anatomy, Royal College of Surgeons of England; etc. 9¾ × 6½ in. Pp. 665, with 309 illustrations. 1954. London: J. & A. Churchill. 55s.

The Foundations of Surgery. By GEORGE PERKINS, *M.C.*, M.Ch., F.R.C.S., Professor of Surgery, London University; Orthopædic Surgeon, St. Thomas's Hospital. 7½ × 4¾ in. Pp. 236 + viii. 1954. Edinburgh: E. & S. Livingstone Ltd. 10s.

Textbook of Chiropody. By MARGARET J. MCKENZIE SWANSON, B.Litt., F.Ch.S., Co-founder of Edinburgh Foot Clinic and School of Chiropody. Second edition. 8½ × 5½ in. Pp. 268 + viii, with 160 illustrations. 1954. Edinburgh: E. & S. Livingstone Ltd. 22s. 6d.

Anesthesia in General Practice. By STUART C. CULLEN, M.D., Chairman, Division of Anesthesiology, Department of Surgery, State University of Iowa Hospitals; Professor of Surgery (Anæsthesiology), State University of Iowa College of Medicine. Fourth edition. 8 × 5½ in. Pp. 312, with 37 illustrations. 1954. Chicago: The Year Book Publishers Inc. (London: Interscience Publishers Ltd.). 38s.

Demonstrations of Operative Surgery. A Manual for General Practitioners, Medical Students, and Nurses. By HAMILTON BAILEY, F.R.C.S., F.A.C.S., F.I.C.S., F.R.S.E., Emeritus Surgeon, Royal Northern Hospital; etc. Second edition. 8½ × 5½ in. Pp. 387 + xii, with 538 illustrations. 1954. Edinburgh: E. & S. Livingstone Ltd. 24s.

Cancer, Diagnosis, Treatment, and Prognosis. By LAUREN V. ACKERMAN, M.D., and JUAN A. DEL REGATO, M.D., Director, Penrose Cancer Hospital, Colorado Springs, Colo. 9¾ × 6¾ in. Pp. 1201, with 702 illustrations. 1954. London: Henry Kimpton. £8 10s.